DIALOG

Set	Items	Description
S1	6159	ALPHAVIRUS?
S2	1347	VENEZUELAN(W)EQUINE(W)ENCEPHALITIS(W)VIRUS
S3	897056	VECTOR? ?
S4	7179	S1 OR S2
S5	1095	S4(S)S3
S6	433325	VACCINE? ? OR IMMUNOGENIC
S7	3971296	CANCER OR TUMOR OR TUMOUR OR NEOPLASTIC OR NEOPLASM
S8	290	S5 AND S6 AND S7
S9	114	S8 NOT PY>1998
S10	113	RD (unique items)
S11	532125	ATTENUATED OR ATTENUATION OR ATTENUATING
S12	0	E2
S13	0	E1
S14	0	E3
S15	105217	"E1"
S16	153426	"E2"
S17	38004	"E3"
S18	228507	S15 OR S16 OR S17
S19	84	S5 AND S11 AND S18
S20	64	S19 NOT S10
S21	21	S20 NOT PY>1998
S22	21	RD (unique items)
S23	0	ALPHAVIRUS(W)26S(W)SUBGENOMIC(W)PROMOTOR
S24	0	ALPHAVIRUS(5N)SUBGENOMIC(5N)PRMOTOR? ?
S25	0	ALPHAVIRUS(5N)SUBGENOMIC(5N)PROMOTOR? ?
S26	6809	26S
S27	253	S4 AND S26
S28	53586	PROMOTOR? ?
S29	2	S27 AND S28
S30	129740	INFLUENZA
S31	283080	HEMAGGLUTININ OR HA
S32	23955	S30(S)S31
S33	112	S5 AND S32
S34	77	S33 NOT (S10 OR S22)
S35	29	S34 NOT PY>1998
S36	17	RD (unique items)
S37	436	AU="MACDONALD G" OR AU="MACDONALD G H"
S38	20	AU="MACDONALD G." OR AU="MACDONALD G.H."
S39	14	AU="MACDONALD GENE" OR AU="MACDONALD GENE H"
S40	46	AU="MARTIN B K"
S41	5	AU="MARTIN B.K."
S42	86	AU="MARTIN BRIAN" OR AU="MARTIN BRIAN K"
S43	337	AU="JOHNSTON R E"
S44	57	AU="JOHNSTON R.E."
S45	57	AU="TING JENNY" OR AU="TING JENNY P Y" OR AU="TING JENNY P-Y" OR AU="TING JENNY PAN YUN" OR AU="TING JENNY PAN YUNG" OR AU="TING JENNY PAN-YUN" OR AU="TING JENNY PAN-YUNG"
S46	1040	S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45
S47	88	S46 AND (S5 OR S6 OR S7)
S48	65	RD (unique items)

?

10/3,AB/1 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00311198
IDENTIFYING NO.: 1Z01HG00077-03 AGENCY CODE: CRISP
TRANSCRIPTION TARGETING/CONDITIONAL EXPRESSION OF TRANSGENE-- CANCER **IMMUNOTHERAP**
PRINCIPAL INVESTIGATOR: XANTHOPOULOS, K G
ADDRESS: NHGRI, NIH
SPONSORING ORG.: NATIONAL HUMAN GENOME RESEARCH INSTITUTE
FY : 2000
SUMMARY: The Gene Expression and Control Unit of the Clinical Gene Therapy Branch (CGTB) is focused on two areas of research (i) Molecular Mechanisms of Transcriptional Regulation and Targeting and (ii) Gene Therapy of **Cancer** and Metabolic Disorders The study of transcription regulatory molecules is of seminal importance because it provides information of the fundamental mechanisms that regulate spatial and developmental gene expression in vivo. Our approach is to study the interplay between regulatory sequences and the corresponding transcriptional factors. We are particularly interested in the role of two members of the CCAAT Enhancer Binding Protein (C/EBP) family, C/EBP-alpha and C/EBP-epsilon, in cell proliferation and differentiation of hepatocytes, adipocytes and hematopoietic cells respectively. We study their the functional roles in vivo using homologous recombination for targeted interruption of both genes and for conditional inactivation of C/EBP-alpha. Furthermore, study semi-synthetic cell-specific transcriptional elements for potential use in targeted transcriptional gene therapy strategies. The other major focus of our laboratory is the development of novel **vectors** for **cancer** gene immunotherapy and controllable methods of gene expression of transgenes in vivo. **Cancer** immunotherapy holds great promise because it may facilitate the use of therapeutic **vaccines** for the treatment of tumors. We seek to generate a combined approach which may have high potential therapeutic value for several human cancers. This strategy is based on (i) highly efficient **alphaviruses** , e.g. Semliki Forest Virus (SFV) and (ii) hybrid Adenoviral/SFV chimeric **vectors** . SFV has several advantages over existing **vectors** : efficient autocatalytic cytoplasmic replication, late onset of cytopathogenic effects, broad host range and genome of positive polarity. We envisaged that the combination of localized high levels of expression of HSV-TK with a "programmed" oncolycate due to the cytotoxicity of SFV particles will have a synergistic effect in promoting rigorous **tumor** rejection and enhancement of long-term survival of our animals in an experimental malignant glioma model.

10/3,AB/2 (Item 1 from file: 315)
DIALOG(R)File 315:ChemEng & Biotec Abs

439076 CEABA Accession No.: 29-06-011092 DOCUMENT TYPE: Journal
Title: AlphaVax focuses on novel virus-based technology.
CORPORATE SOURCE: AlphaVax Durham, NC USA
JOURNAL: Pharmaceutical Business News, Volume: 14, Issue: 310, Page(s): 17
ISSN: 09560661
PUBLICATION DATE: 11 Feb 1998 (980211) LANGUAGE: English
ABSTRACT: AlphaVax has been set up in Durham, NC, USA, to commercialize a novel virus-based technology intended for **vaccine** and gene therapy applications. The Alpha Vax **Vector** System (VAS) is derived from the **Venezuelan equine encephalitis virus** . The company says the

vector exhibits high **vector** -driven antigen expression levels and natural targeting to immune system cells. Applications include **vaccines** for infectious diseases and **cancer** , gene therapy, veterinary **vaccines** and the manufacture of **vaccine** intermediates and therapeutic proteins. The first partnership -with Wyeth-Lederle **Vaccines** and Paediatrics -comprises exclusive licences relating to herpes simplex viruses, parainfluenza viruses, human papilloma virus and respiratory syncytial virus.

10/3,AB/4 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

130094470 CA: 130(8)94470f PATENT
Improved methods for inducing an immune response
INVENTOR(AUTHOR): Warnier, Guy; Uyttenhove, Catherine; Boon-Falleur, Thierry
LOCATION: USA
ASSIGNEE: Ludwig Institute for Cancer Research
PATENT: PCT International ; WO 9858956 A2 DATE: 19981230
APPLICATION: WO 98US12894 (19980619) *US 880979 (19970623)
PAGES: 61 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/00A
DESIGNATED COUNTRIES: AU; CA; CN; JP; KR; NZ DESIGNATED REGIONAL: AT; BE ; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

10/3,AB/5 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

123104352 CA: 123(9)104352r PATENT
Alphavirus vectors for the expression of foreign genes in animal cells for therapeutic use
INVENTOR(AUTHOR): Dubensky, Thomas W., Jr.; Ibanez, Carlos E.; Chang, Stephen M. W.; Jolly, Douglas J.; Driver, David A.; Polo, John M.
LOCATION: USA
ASSIGNEE: Viagene, Inc.
PATENT: PCT International ; WO 9507994 A2 DATE: 950323
APPLICATION: WO 94US10469 (940915) *US 122791 (930915) *US 198450 (940218)
PAGES: 260 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/85A; A61K-035/76B; C12N-005/10B; A61K-048/00B DESIGNATED COUNTRIES: AM; AU; BB; BG; BR; BY; CA; CN; CZ; FI; GE; HU; JP; KE; KG; KP; KR; KZ; LK; LT; MG; MN; MW; NO; NZ; PL; RO; RU; SD; SI; SK; TJ; TT; UA; UZ; VN
DESIGNATED REGIONAL: KE; MW; SD; AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

10/3,AB/7 (Item 2 from file: 348)
DIALOG(R)File 348:European Patents

00891422
Recombinant alphavirus vectors
Rekombinante Alphavirus-Vektoren
Vecteurs composes d'alphavirus recombinants
PATENT ASSIGNEE:
CHIRON CORPORATION, (572530), 4560 Horton Street, Emeryville, California 94608, (US), (applicant designated states:

AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Dubensky, Thomas W. Jr., P.O.Box 802elino, Del Mar, CA 92014, (US)
Ibanez, Carlos E., 13592 Millpond Way, San Diego, CA 92129, (US)
Chang, Stephen M.W., 12912 Camino del Valle, Poway, California 92064, (US)
Jolly, Douglas J., 277 Hillcrest Drive, leucadia, CA 92024, (US)
Driver, David A., 5142 Biltmore St., San Diego, CA 92117, (US)
Polo, John M., 221 Witham Road, Encinitas, CA 92024, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 814154 A2 971229 (Basic)
EP 814154 A3 981014
APPLICATION (CC, No, Date): EP 97113527 940915;
PRIORITY (CC, No, Date): US 122791 930915; US 198450 940218
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 694070 (EP 949292213)
INTERNATIONAL PATENT CLASS: C12N-007/01; C12N-015/86;

ABSTRACT EP 814154 A2
The present invention provides expression cassettes for expression of **alphavirus** structural proteins and host cells, including packaging cells for packaging of **alphavirus** RNA **vectors** , containing such expression cassettes.
ABSTRACT WORD COUNT: 29

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9712W3	740
SPEC A	(English)	9712W3	61597
Total word count - document A			62337
Total word count - document B			0
Total word count - documents A + B			62337

10/3,AB/8 (Item 3 from file: 348)
DIALOG(R)File 348:European Patents

00762297
Recombinant alphavirus vectors
Rekombinanter Alphavirus Vektor
Vecteurs composes d'alphavirus recombinants
PATENT ASSIGNEE:
CHIRON VIAGENE, INC., (2076910), 4560 Horton Street, Emeryville, California 94608, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Dubensky, Thomas W. Jr., 12729 Via Felino, Del Mar, CA 92014, (US)
Ibanez, Carlos E., 13592 Millpond Way, San Diego, CA 92129, (US)
Chang, Stephen M.W., 9838 Via Cacares, San Diego, CA 92129, (US)
Jolly, Douglas J., 277 Hillcrest Drive, Leucadia, CA 92024, (US)
Driver, David A., 5142 Biltmore St., San Diego, CA 92117, (US)
Polo, John M., 3910 Haines Street, No. 4, San Diego, CA 92109, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)

PATENT (CC, No, Kind, Date): EP 716148 A2 960612 (Basic)
EP 716148 A3 970102
APPLICATION (CC, No, Date): EP 95115460 940915;
PRIORITY (CC, No, Date): US 122791 930915; US 198450 940218
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 694070 (EP 949292213)
INTERNATIONAL PATENT CLASS: C12N-015/86;

ABSTRACT EP 716148 A2
The present invention provides composition and methods for utilizing recombinant **alphavirus vectors** .
ABSTRACT WORD COUNT: 20

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	198
SPEC A	(English)	EPAB96	54363
Total word count - document A			54561
Total word count - document B			0
Total word count - documents A + B			54561

10/3,AB/9 (Item 4 from file: 348)
DIALOG(R)File 348:European Patents

00756442
Recombinant alphavirus vectors
Rekombinanter Alphavirus Vektor
Vecteurs composes d'alphavirus recombinants
PATENT ASSIGNEE:
CHIRON VIAGENE, INC., (2076910), 4560 Horton Street, Emeryville, California 94608, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Dubensky, Thomas W. Jr., 12729 Via Felino, Del Mar, CA 92014, (US)
Ibanez, Carlos E., 13592 Millpond Way, San Diego, CA 92129, (US)
Chang, Stephen M.W., 9838 Via Cacares, San Diego, CA 92129, (US)
Jolly, Douglas H., 277 Hillcrest Drive, Leucadia, CA 92024, (US)
Driver, David H., 5142 Biltmore St., San Diego, CA 92117, (US)
Polo, John M., 221 Witham Road, Encinitas, CA 92024, (US)
LEGAL REPRESENTATIVE:
Brasnett, Adrian Hugh et al (73111), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5LX, (GB)
PATENT (CC, No, Kind, Date): EP 711829 A2 960515 (Basic)
EP 711829 A3 970709
APPLICATION (CC, No, Date): EP 95115459 940915;
PRIORITY (CC, No, Date): US 122791 930915; US 198450 940218
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 694070 (EP 949292213)
INTERNATIONAL PATENT CLASS: C12N-007/01; C12N-015/86;

ABSTRACT EP 711829 A2
The present invention provides compositions and methods for utilizing recombinant **alphavirus vectors** .
ABSTRACT WORD COUNT: 20

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	1169
SPEC A	(English)	EPAB96	54372
Total word count - document A			55541
Total word count - document B			0
Total word count - documents A + B			55541

10/3,AB/11 (Item 1 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00613502
IMPROVED METHODS FOR INDUCING AN IMMUNE RESPONSE
PROCEDES AMELIORES VISANT A INDUIRE UNE REPONSE IMMUNITAIRE
Patent Applicant/Assignee:
LUDWIG INSTITUTE FOR **CANCER** RESEARCH, LUDWIG INSTITUTE FOR CANCER RESEARCH , 605 Third Avenue, New York, NY 10158 , US
Inventor(s):
WARNIER Guy, WARNIER, Guy , Institute Ludwig pour la Recherche sur le Cancer, Avenue Hippocrate 74, UCL 7459, B-1200 Brussels , BE
UYTTENHOVE Catherine, UYTTENHOVE, Catherine , Institute Ludwig pour la Recherche sur le Cancer, Avenue Hippocrate 74, UCL 7459, B-1200 Brussels , BE
BOON-FALLEUR Thierry, BOON-FALLEUR, Thierry , Institute Ludwig pour la Recherche sur le Cancer, Avenue Hippocrate 74, UCL 7459, B-1200 Brussels , BE
Patent and Priority Information (Country, Number, Date):
Patent: WO 9858956 A2 19981230
Application: WO 98US12894 19980619 (PCT/WO US9812894)
Priority Application: US 97880979 19970623
Designated States: AU CA CN JP KR NZ AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Filing Language: English
Fulltext Word Count: 17998

English Abstract
This invention relates to improved methods for modulating an immune response against an antigen using adenoviruses which express the antigen for priming immunization and antigen peptides for booster immunizations. Preferably the peptides are combined with QS21/MPL adjuvant. In particular, immunization methods for **tumor** antigens are provided. Kits for immunization are also provided.

French Abstract
L'invention concerne des procedes ameliores destines a moduler une reponse immunitaire contre un antigene, au moyen d'adenovirus exprimant cet antigene et permettant d'amorcer l'immunisation, et de peptides antigeniques favorisant cette immunisation. Ces peptides sont de preferences combines a un adjuvant QS21/MPL. L'invention concerne plus particulierement des procedes d'immunisation contre des antigenes tumoraux, ainsi que des kits d'immunisation.

10/3,AB/19 (Item 9 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00597092
NEW APPLICATIONS OF GENE THERAPY TECHNOLOGY
NOUVELLES APPLICATIONS DE LA TECHNIQUE DE LA THERAPIE GENIQUE
Patent Applicant/Assignee:
ARIAD GENE THERAPEUTICS INC, ARIAD GENE THERAPEUTICS, INC. , 26 Landsdowne Street, Cambridge, MA 02139-4234 , US
GILMAN Michael Z
Inventor(s):
ARIAD GENE THERAPEUTICS INC, ARIAD GENE THERAPEUTICS, INC. , 26 Landsdowne Street, Cambridge, MA 02139-4234 , US
GILMAN Michael Z
Patent and Priority Information (Country, Number, Date):
Patent: WO 9839418 A1 19980911
Application: WO 98US4525 19980309 (PCT/WO US9804525)
Priority Application: US 9713014 19970307; US 97400643 19970308
Designated States: AU CA AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Filing Language: English
Fulltext Word Count: 14470

English Abstract
This invention provides new applications of regulated gene therapy relating to treatment of **cancer** and other disorders.

French Abstract
La presente invention concerne de nouvelles applications de la therapie genique regulee concernant le traitement du **cancer** et d'autres troubles.

10/3,AB/20 (Item 10 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00594512
VECTORS HAVING ENHANCED EXPRESSION, AND METHODS OF MAKING AND USES THEREOF
VECTEURS AYANT UNE EXPRESSION FACILITEE, METHODES DE PRODUCTION ET D'UTILISATION DESDITS VECTEURS
Patent Applicant/Assignee:
VIROGENETICS CORPORATION, VIROGENETICS CORPORATION , 465 Jordan Road, Rensselaer Technology Park, Troy, NY 12180 , US
Inventor(s):
TARTAGLIA James, TARTAGLIA, James , 7 Christina Drive, Schenectady, NY 12303 , US
COX William I, COX, William, I. , 1379 Maple Trail, Sand Lake, NY 12153 , US
GETTIG Russell R, GETTIG, Russell, R. , R.D. 2, Box 421C, Averill Park, NY 12018 , US
MARTINEZ Hector, MARTINEZ, Hector , Apartment 9, 15 Park Lane East, Menands, NY 12204 , US
PAOLETTI Enzo, PAOLETTI, Enzo , 297 Murray Avenue, Delmar, NY 12054 , US
PINCUS Steven E, PINCUS, Steven, E. , 78 Troy Road, East Greenbush, NY 12061 , US
Patent and Priority Information (Country, Number, Date):
Patent: WO 9840501 A1 19980917
Application: WO 98US2669 19980213 (PCT/WO US9802669)
Priority Application: US 97816155 19970312
Designated States: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English

Filing Language: English
Fulltext Word Count: 21393

English Abstract
Disclosed and claimed are vectors having enhanced expression and methods for making and using them. Enhancement of expression is from substantially co-temporal expression of at least one first nucleic acid molecule and at least one second nucleic acid molecule. The second nucleic acid molecule encodes a transcription factor or a translation factor or a transcription factor and a translation factor. The contemporaneous expression can be from operably linking the first and second nucleic molecules to a single promoter, or from operably linking the first nucleic acid molecule to a first promoter and the second nucleic molecule to a second promoter wherein the first and second promoters function substantially contemporaneously. Thus, the first and second nucleic acid molecules can be at the same locus in the vector, or at different loci. The second nucleic acid molecule can encode: one transcription factor or more than one transcription factor; or one translation factor or more than one translation factor; or at least one transcription factor and at least one translation factor. The transcription factor can be from vaccinia H4L, D6, A7, G8R, A1L, A2L, H5R, or combinations thereof. The translation factor can be from a K3L open reading frame, an E3L open reading frame, a VAI RNA, an EBER RNA, a sigma 3 open reading frame, a TRBP open reading frame, or combinations thereof. The vector can be a poxvirus such as an attenuated poxvirus, e. g., NYVAC, or ALVAC.

French Abstract
On decrit des vecteurs ayant une expression facilitee, ainsi que des methodes de production et d'utilisation desdits vecteurs. La facilitation d'expression decoule d'une expression sensiblement contemporaine d'au moins une premiere molecule d'acide nucleique et d'au moins une deuxieme molecule d'acide nucleique. La deuxieme molecule d'acide nucleique code un facteur de transcription et/ou un facteur de traduction. L'expression contemporaine peut decouler d'une liaison fonctionnelle de la premiere molecule et de la deuxieme molecule d'acide nucleique avec un seul promoteur, ou d'une liaison fonctionnelle de la premiere molecule d'acide nucleique avec un premier promoteur, et de la deuxieme molecule d'acide nucleique avec un deuxieme promoteur, le premier promoteur et le deuxieme promoteur fonctionnant de maniere sensiblement contemporaine. Ainsi, la premiere molecule et la deuxieme molecule d'acide nucleique peuvent se trouver sur le meme site actif dans le vecteur, ou sur des sites differents. La deuxieme molecule d'acide nucleique peut coder un ou plusieurs facteurs de transcription, un ou plusieurs facteurs de traduction, ou au moins un facteur de transcription et au moins un facteur de traduction. Le facteur de transcription peut etre issu de la **vaccine** H4L, D6, A7, G8R, A1L, A2L, H5R, ou une combinaison de ces elements. Le facteur de traduction peut etre issu d'un cadre ouvert de lecture K3L, d'un cadre ouvert de lecture E3L, d'un ARN VAI, d'un ARN EBER, d'un cadre ouvert de lecture d'un facteur sigma 3, d'un cadre ouvert de lecture TRBP, ou d'une combinaison de ces elements. Le vecteur peut etre un poxvirus tel que qu'un poxvirus attenue (NYVAC ou ALVAC, par exemple).

10/3,AB/22 (Item 12 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00590432
POLYNUCLEOTIDE VACCINE **FORMULATIONS**

FORMULES DE VACCINS A BASE DE POLYNUCLEOTIDES

Patent Applicant/Assignee:
MERCK & CO INC, MERCK & CO., INC. , 126 East Lincoln Avenue, Rahway, NJ 07065 , US
Inventor(s):
VOLKIN David B, VOLKIN, David, B. , 126 East Lincoln Avenue, Rahway, NJ 07065 , US
EVANS Robert K, EVANS, Robert, K. , 126 East Lincoln Avenue, Rahway, NJ 07065 , US
ULMER Jeffrey B, ULMER, Jeffrey, B. , 126 East Lincoln Avenue, Rahway, NJ 07065 , US
CAULFIELD Michael J, CAULFIELD, Michael, J. , 126 East Lincoln Avenue, Rahway, NJ 07065 , US

Patent and Priority Information (Country, Number, Date):
Patent: WO 9835562 A1 19980820
Application: WO 98US2414 19980213 (PCT/WO US9802414)
Priority Application: US 9738194 19970214; GB 975460 19970317
Designated States: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE GW HU ID IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Filing Language: English
Fulltext Word Count: 18441

English Abstract
The present invention relates to a novel **vaccine** formulation comprising nucleic acid molecules and a mineral-based adjuvant provided in a biologically effective concentration so as to improve induction of an immune response subsequent to vaccination which correlates to expression of one or more specific antigens encoded by the nucleic acid molecule.

French Abstract
L'invention porte sur une nouvelle formule de vaccin comportant des molecules d'acide nucleique et un adjuvant a base minerale a une concentration a efficacite biologique ameliorant l'induction de la reaction immunitaire suite a une vaccination, en correlation avec l'expression d'un ou plusieurs antigenes specifiques codes par la molecule d'acide nucleique.

10/3,AB/40 (Item 30 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00537258
RECOMBINANT ALPHAVIRUS **BASED** VECTORS **WITH REDUCED INHIBITION OF CELLULAR MACROMOLECULAR SYNTHESIS**
VECTEURS A BASE D'ALPHAVIRUS DE RECOMBINAISON, PRESENTANT UNE INHIBITION REDUITE DE LA SYNTHESE MACROMOLECULAIRE CELLULAIRE

Patent Applicant/Assignee:
CHIRON VIAGENE INC, CHIRON VIAGENE, INC., 4560 Horton Street, Emeryville, CA 946082916, US
WASHINGTON UNIVERSITY, WASHINGTON UNIVERSITY, One Brookings Drive, St. Louis, MO 63130, US
Inventor(s):
DUBENSKY Thomas W Jr, DUBENSKY, Thomas, W., Jr., P.O. Box 675205, Rancho Santa Fe, CA 92067, US
POLO John M, POLO, John, M., 221 Witham Road, Encinitas, CA 92024, US
BELLI Barbara A, BELLI, Barbara, A., 5850 Despejo Place, San Diego, CA

92124, US
SCHLESINGER Sondra, SCHLESINGER, Sondra, 6320 McPherson Street, St. Louis, MO 63105, US
DRYGA Sergey A, DRYGA, Sergey A., 6334 Southwood Avenue &3, St. Louis, MO 63105, US
FROLOV Ilya, FROLOV, Ilya, 7515 Cromwell Drive &2SE, St. Louis, MO 63105, US

Patent and Priority Information (Country, Number, Date):
Patent: WO 9738087 A2 19971016
Application: WO 97US6010 19970404 (PCT/WO US9706010)
Priority Application: US 96628594 19960405; US 96668953 19960624; US 96679640 19960712
Designated States: AL AM AT AU BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 69561

English Abstract
Isolated nucleic acid molecules are disclosed, comprising an **alphavirus** nonstructural protein gene which, when operably incorporated into a recombinant **alphavirus** particle, eukaryotic layered **vector** initiation system, or RNA **vector** replicon, has a reduced level of **vector** specific RNA synthesis, as compared to wildtype, and the same or greater level of proteins encoded by RNA transcribed from the viral junction region promoter, as compared to a wildtype recombinant **alphavirus** particle. Also disclosed are RNA **vector** replicons, **alphavirus** **vector** constructs, and eukaryotic layered **vector** initiation systems which contain the aboveidentified nucleic acid molecules.

French Abstract
L'invention concerne des molecules d'acide nucleique isolees comportant un gene proteique non structural d'alphavirus qui, lorsqu'il est incorpore fonctionnellement dans une particule d'alphavirus de recombinaison, un systeme d'initiation de vecteur stratifie eucaryote, ou bien un replicon de vecteur d'ARN, presente un niveau reduit de synthese d'ARN specifique du vecteur, compare au type sauvage, et un niveau identique ou superieur de proteines codees par l'ARN transcrit a partir du promoteur de region de jonction viral, compare a une particule d'alphavirus de recombinaison de type sauvage. L'invention concerne egalement des replicons de vecteur d'ARN, des produits de recombinaison de vecteur d'alphavirus, et des systemes d'initiation de vecteur stratifie eucaryote qui contiennent les molecules d'acide nucleique precitees.

10/3,AB/45 (Item 35 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00523846
IMMUNOSTIMULATION MEDIATED BY GENE-MODIFIED DENDRITIC CELLS
IMMUNOSTIMULATION A MEDIATION PAR CELLULES DENDRITIQUES MODIFIEES PAR DES GENES
Patent Applicant/Assignee:
CHIRON VIAGENE INC
Inventor(s):
SONG Elizabeth S

CHADA Sunil
LEE Virginia
JOLLY Douglas J
Patent and Priority Information (Country, Number, Date):
Patent: WO 9724447 A1 19970710
Application: WO 96US20105 19961220 (PCT/WO US9620105)
Priority Application: US 96581867 19960102; US 96587285 19960116; US 96772010 19961219
Designated States: CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 15533

English Abstract
Compositions and methods useful for stimulating an immune response against one or more disease associated antigens by genetically modifying dentritic cells in vivo or ex vivo are provided. These compositions and methods allow for administration of lower dosages of gene delivery vehicles in order to achieve levels of immune stimulation comparable to those obtainable by conventional methods. Alternatively, administration of conventional dosages of gene delivery vehicles will enhance the resultant immune response.

French Abstract
L'invention concerne des compositions et des methodes utiles pour provoquer une reponse immunitaire contre des antigenes associes a une ou plusieurs maladies, par la modification genetique de cellules dendritiques in vivo ou ex vivo. Ces compositions et ces methodes permettent d'administrer des doses plus faibles de vehicules d'apport de genes afin d'obtenir des niveaux de stimulation immunitaire comparables a ceux obtenus par les methodes classiques. L'administration de doses classiques de vehicules d'apport de genes peut par ailleurs ameliorer la reponse immunitaire obtenue.

10/3,AB/46 (Item 36 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00523845
GENE DELIVERY VEHICLE-TARGETING LIGANDS
LIGANDS DE CIBLAGE DE VEHICULES POUR L'APPORT DE GENES
Patent Applicant/Assignee:
CHIRON VIAGENE INC
Inventor(s):
CHADA Sunil
BANKS Theresa
MOORE Margaret D
CHANG Stephen M W
Patent and Priority Information (Country, Number, Date):
Patent: WO 9724446 A2 19970710
Application: WO 96US20295 19961220 (PCT/WO US9620295)
Priority Application: US 95580541 19951229; US 959411 19951229
Designated States: CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 13912

English Abstract
Fusion proteins composed of an MHC Class I molecule, MHC Class II molecule, or 'beta'2 microglobulin, and a targeting ligand are disclosed. Also disclosed are nucleic acid molecules which encode such fusion proteins as well as suitable expression cassettes and host cells. Also

provided are methods for targeting a gene delivery vehicle to a selected cell type utilizing gene delivery vehicles which contain on their surfaces one of the above-mentioned fusion proteins.

French Abstract
La presente invention concerne des proteines fusionnees constituees par une molecule CMH de classe I ou II ou une microglobuline 'beta'2; l'invention concerne aussi un ligand de ciblage. L'invention concerne, de plus, des molecules d'acide nucleique qui codent de telles proteines fusionnees ainsi que des cassettes d'expression appropriees et des cellules hotes. Elle concerne egalement des procedes de ciblage d'un vehicule d'apport de genes sur un type de cellule selectionne, au moyen de vehicules d'apport de genes qui contiennent, sur leurs surfaces, l'une des proteines fusionnees precitees.

10/3,AB/54 (Item 44 from file: 349)

00425936
METHODS AND COMPOSITIONS FOR TREATMENT OF SOLID TUMORS IN VIVO
PROCEDES ET COMPOSTIONS DE TRAITEMENT DE TUMEURS SOLIDES IN VIVO
Patent Applicant/Assignee:
CHIRON VIAGENE INC
Inventor(s):
BURROWS Francis J
FONG Timothy C
POLO John M
DUBENSKY Thomas W Jr
JOLLY Douglas J
Patent and Priority Information (Country, Number, Date):
Patent: WO 9621416 A2-A3 19960718
Application: WO 95US16855 19951222 (PCT/WO US9516855)
Priority Application: US 94368574 19941230
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UZ VN AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 44632
English Abstract
The present invention provides compositions and methods for treatment of solid tumors with gene therapy utilizing recombinant viral vectors that express polypeptides which selectively initiate irreversible coagulation of blood in the **tumor** vasculature, inhibit **tumor** neovascularization, are capable of activating a non-toxic agent into a toxic agent within the **tumor** vascular wall causing destruction of the vascular bed and absorb or metabolize nutrients in the blood being supplied to the **tumor** . The production of these polypeptides by transduced cells in or adjacent to the blood vessels of the **tumor** result in the death of **tumor** cells.

French Abstract
L'invention concerne des compositions et des procedes de traitement de tumeurs solides par therapie genique au moyen de vecteurs viraux recombinants exprimant des polypeptides qui declenchent selectivement une coagulation irreversible du sang dans le systeme vasculaire de la tumeur, inhibent la neoformation de vaisseaux sanguins dans la tumeur, sont capables d'activer un agent non toxique afin de le transformer en agent toxique a l'interieur de la paroi vasculaire de la tumeur, ce qui provoque la destruction du lit vasculaire et absorbe ou metabolise les produits nutritifs du sang alimentant la tumeur. La production de ces

polypeptides par des cellules transduites dans les vaisseaux sanguins ou en position contigue a ces derniers, a pour effet de provoquer la mort des cellules cancereuses.

10/3,AB/57 (Item 47 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00425625
COMBINATION GENE DELIVERY VEHICLES
COMBINAISON DE VECTEURS D'ADMINISTRATION DE GENES
Patent Applicant/Assignee:
CHIRON VIAGENE INC
Inventor(s):
JOLLY Douglas J
MONTISANO Dominic
Patent and Priority Information (Country, Number, Date):
Patent: WO 9621015 A2-A3 19960711
Application: WO 95US16964 19951222 (PCT/WO US9516964)
Priority Application: US 94368210 19941230
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KR KZ LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 53455

English Abstract
The combination of multiple, i.e., two or more, gene delivery vehicles ("GDVs") with pharmaceutically acceptable carrier or diluent to provide a pharmaceutically acceptable composition, and the administration of such a composition to an animal. The invention provides numerous advantages over previous methods of treating diseases or other pathogenic agents that included the use of a GDV, such as control of the level of expression of different genes carried by different GDVs, for example when it is preferred that the elicited response be predominantly against a gene product from one GDV, or if an immediate response is required from one GDV's gene product and a delayed or priming response is required from the other.

French Abstract
Combinaison de vecteurs multiples (a savoir au moins deux) d'administration de genes (GDV) avec un vehicule ou un diluant pharmaceutiquement acceptables, pour la production d'une composition pharmaceutiquement acceptable, et administration de ladite composition a un animal. L'invention presente de nombreux avantages par rapport a d'anciens procedes de traitement de maladies ou d'autres agents pathogenes impliquant l'utilisant de GDV, tels que la regulation du niveau d'expression de differents genes portes par differents GDV, par exemple, quand il est preferable que la reaction recherchee soit dirigee particulierement contre un produit genique provenant d'un GDV ou dans le cas ou une reaction immediate est attendue d'un produit genique d'un GDV et ou une reaction de retard ou d'amorcage est attendue de l'autre.

10/3,AB/61 (Item 51 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00421833
RECOMBINANT ALPHAVIRUS VECTORS

VECTEURS D'ALPHAVIRUS DE RECOMBINAISON
Patent Applicant/Assignee:
CHIRON VIAGENE INC
Inventor(s):
DUBENSKY Thomas W Jr
POLO John M
IBANEZ Carlos E
CHANG Stephen M W
JOLLY Douglas J
DRIVER David A
BELLI Barbara A
Patent and Priority Information (Country, Number, Date):
Patent: WO 9617072 A2-A3 19960606
Application: WO 95US15490 19951130 (PCT/WO US9515490)
Priority Application: US 94348472 19941130; US 95376184 19950118; US 95405827 19950315
Designated States: AU CA JP MX AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 83340

English Abstract
The present invention provides composition and methods for utilizing recombinant **alphavirus vectors** .

French Abstract
L'invention concerne une composition et des procedes utilisant des vecteurs d'alphavirus de recombinaison.

10/3,AB/63 (Item 53 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00400215
ALPHAVIRUS **EXPRESSION** VECTOR
VECTEUR D'EXPRESSION DE L'ALPHAVIRUS
Patent Applicant/Assignee:
BIOPTION AB
SJOBERG Mathilda
SUOMALAINEN Maarit
GAROFF Henrik
Inventor(s):
SJOBERG Mathilda
SUOMALAINEN Maarit
GAROFF Henrik
Patent and Priority Information (Country, Number, Date):
Patent: WO 9531565 A1 19951123
Application: WO 95SE558 19950517 (PCT/WO SE9500558)
Priority Application: SE 941709 19940518
Designated States: AU CA FI JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 8499
English Abstract
The present invention is directed to **alphavirus** expression **vectors** comprising at least part of an **alphavirus** genome and heterologous RNA inserted downstream of an **alphavirus** base sequence having translation enhancing activity. Such **vectors** can be used to achieve enhanced levels of expression of DNA or cDNA coding for a desired product and being complementary to said heterologous RNA after introduction of said **vector**

in eukaryotic cells in cell culture or in a living body. The expression product may have therapeutical or prophylactic activity.

French Abstract
La presente invention concerne des vecteurs d'expression de l'alphavirus comportant au moins une partie d'un genome d'alphavirus et un ARN heterologue insere en aval d'une sequence de base d'alphavirus presentant une activite facilitant la traduction. De tels vecteurs s'utilisent pour obtenir des niveaux ameliores d'expression d'ADN ou d'ADNc codant pour un produit desire et etant complementaires dudit ARN heterologue apres introduction dudit vecteur dans des cellules eucaryotes dans une culture cellulaire ou dans un organisme vivant. Le produit d'expression peut presenter une activite therapeutique ou prophylactique.

10/3,AB/64 (Item 54 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00396148
ALPHAVIRUS RNA AS CARRIER FOR VACCINES
ARN D'ALPHAVIRUS UTILISE COMME VECTEUR DE VACCINS
Patent Applicant/Assignee:
SMITHKLINE BEECHAM BIOLOGICALS (SA)
BIOPTION AB
DALEMANS Wilfried
BRUCK Claudine
LILJESTROM Peter Torsten
Inventor(s):
DALEMANS Wilfried
BRUCK Claudine
LILJESTROM Peter Torsten
Patent and Priority Information (Country, Number, Date):
Patent: WO 9527069 A1 19951012
Application: WO 95EP1080 19950322 (PCT/WO EP9501080)
Priority Application: GB 946498 19940331
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 3217

English Abstract
Vaccine compositions are provided that employ alphavirus RNA molecules containing exogenous RNA sequences encoding an antigen for direct administration to a patient.

French Abstract
La presente invention concerne des compositions vaccinales utilisant des molecules d'ARN d'alphavirus, lesquelles molecules contiennent des sequences d'ARN exogenes codant un antigene. Ces compositions vaccinales sont directement administrables a un patient.

10/3,AB/65 (Item 55 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00396129
ALPHAVIRUS **cDNA** VECTORS

VECTEURS D'ADNc D'ALPHAVIRUS
Patent Applicant/Assignee:
BIOPTION AB
LILJESTROM Peter
GAROFF Henrik
Inventor(s):
LILJESTROM Peter
GAROFF Henrik
Patent and Priority Information (Country, Number, Date):
Patent: WO 9527044 A1 19951012
Application: WO 95SE343 19950330 (PCT/WO SE9500343)
Priority Application: SE 941091 19940331
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SG SI SK TJ TT UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 6145
English Abstract
The present invention is related to polynucleotide molecules and to their use for production of desired products after introduction into human or animal cells. In addition, the present invention is concerned with pharmaceutical compositions comprising said polynucleotide molecules and their use in prophylactic or therapeutic treatment methods. The present invention is also related to use of such polynucleotide molecules in animals to achieve expression of desired products, which can be recovered from the animal but do not give rise to any beneficial, e.g. therapeutical, activity in the said animal. More specifically, the present invention is directed to **alphavirus** cDNA **vectors** comprised of recombinant cDNA consisting of cDNA derived from an **alphavirus** and heterologous, i.e. foreign, cDNA coding for a desired substance.

French Abstract
L'invention concerne des molecules de polynucleotides et leur utilisation, afin de preparer des produits determines apres introduction dans les cellules de l'homme ou de l'animal. De plus, l'invention concerne des compositions pharmaceutiques comprenant lesdites molecules de polynucleotides et leur utilisation dans des procedes de traitement prophylactiques ou therapeutiques. Elle concerne egalement l'utilisation de ces molecules de polynucleotides chez l'animal, afin de realiser l'expression desdits produits, qu'on peut recuperer depuis ledit animal mais qui n'occasionnent aucune activite benefique, c'est-a-dire therapeutique chez ledit animal. L'invention concerne, plus specifiquement, des vecteurs d'ADNc d'alphavirus composes d'ADNc recombinant consistant en de l'ADNc derive d'un alphavirus et en de l'ADNc heterologue, c'est-a-dire etranger, codant pour une substance voulue.

10/3,AB/67 (Item 57 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00376742
RECOMBINANT ALPHAVIRUS VECTORS
VECTEURS COMPOSES D'ALPHAVIRUS RECOMBINANTS
Patent Applicant/Assignee:
VIAGENE INC
Inventor(s):
DUBENSKY Thomas W Jr
IBANEZ Carlos E

CHANG Stephen M W
JOLLY Douglas J
DRIVER David A
POLO John M
Patent and Priority Information (Country, Number, Date):
Patent: WO 9507994 A2-A3 19950323
Application: WO 94US10469 19940915 (PCT/WO US9410469)
Priority Application: US 93122791 19930915; US 94198450 19940218
Designated States: AM AU BB BG BR BY CA CN CZ FI GE HU JP KE KG KP KR KZ LK LT MG MN MW NO RO RU SD SI SK TJ TT UA UZ VN KE MW SD AT BE CH DE DK ES FR GB GR IE IT NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 73362

English Abstract
The present invention provides composition and methods for utilizing recombinant **alphavirus vectors** .

French Abstract
La presente invention se rapporte a une composition et a des procedes d'utilisation de vecteurs composes d'alphavirus recombinants.

10/3,AB/69 (Item 59 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00347641
VECTOR TO DELIVER AND EXPRESS FOREIGN GENE
VECTEUR TRANSPORTANT ET EXPRIMANT UN GENE ETRANGER
Patent Applicant/Assignee:
COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION
WALKER Peter John
PREHAUD Christophe Jean
COWLEY Jeff Alexander
Inventor(s):
WALKER Peter John
PREHAUD Christophe Jean
COWLEY Jeff Alexander
Patent and Priority Information (Country, Number, Date):
Patent: WO 9408022 A1 19940414
Application: WO 93AU495 19930928 (PCT/WO AU9300495)
Priority Application: AU 924974 19920928
Designated States: AT AU BB BG BR BY CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU LV MG MN NO NZ PL PT RO RU SD SE SK UA US UZ VN AT BE CH DE DK ES FR GB GR IE IT NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 10498

English Abstract
A vector for delivering a foreign gene to a target cell for expression of the foreign gene is provided. The vector comprises a (-) sense RNA genome contained within a ribonucleoprotein complex within a virus-like particle constituted from structural proteins of a (-) sense RNA virus. The (-) sense RNA genome includes one or more foreign genes but does not include genes for replication of the (-) sense RNA virus. Methods of preparing the vector are disclosed, as well as pharmaceutical compositions containing the vector, and methods of delivering the expression product of the foreign gene to a target cell.

French Abstract

Vecteur apportant un gene etranger jusqu'a une cellule cible afin d'exprimer le gene etranger. Le vecteur comprend un genome d'ARN antisens contenu dans un complexe de ribonucleoproteine dans une particule analogue a un virus constituee des proteines de structure d'un virus a ARN antisens. Le genome d'ARN antisens comprend un ou plusieurs genes etrangers, mais ne comprend pas des genes permettant la replication du virus a ARN antisens. Des procedes de preparation du vecteur sont decrits, ainsi que des compositions pharmaceutiques contenant ce dernier et des procedes permettant d'apporter le produit d'expression du gene etranger a une cellule cible.

10/3,AB/76 (Item 3 from file: 654)

02867541

Utility
GENETIC IMMUNIZATION
[**Vaccines** of DNA sequences encoding pathogens, oncogenes and other proteins causing diseases]

PATENT NO.: 5,830,876
ISSUED: November 03, 1998 (19981103)
INVENTOR(s): Weiner, David B., Merion, PA (Pennsylvania), US (United States of America)
Williams, William V., Havertown, PA (Pennsylvania), US (United States of America)
Wang, Bin, Havertown, PA (Pennsylvania), US (United States of America)
ASSIGNEE(s): The Trustees of the University of Pennsylvania, (A U.S. Company or Corporation), Philadelphia, PA (Pennsylvania), US (United States of America)
The Wistar Institute, (A U.S. Company or Corporation), Philadelphia, PA (Pennsylvania), US (United States of America)
[Assignee Code(s): 64664; 92890]
APPL. NO.: 8-453,349
FILED: May 30, 1995 (19950530)

CROSS REFERENCE TO RELATED APPLICATIONS

This is a continuation of application Ser. No. 08-029,336, filed Mar. 11, 1993, now abandoned, which is a continuation-in-part of application Ser. No. 08-008,342, filed Jan. 26, 1993, now abandoned.

FULL TEXT: 2904 lines

ABSTRACT

A method of immunizing an individual against pathogen is disclosed. Also disclosed is a method of treating an individual who has a hyperproliferative disease, or of treating an individual who is infected by a pathogen. Specifically, the individual is injected with bupivacaine along with DNA in an expressible form, the DNA encoding an antigen. The encoded antigen can be from a protein from the pathogen or from a protein associated with the hyperproliferative disease.

10/3,AB/79 (Item 6 from file: 654)

02853259

Utility

GENETIC IMMUNIZATION

[DNA sequence linked to regulatory sequences controlling expression of the DNA sequence, bupivacaine or derivatives]

PATENT NO.: 5,817,637
ISSUED: October 06, 1998 (19981006)
INVENTOR(s): Weiner, David B., Merion, PA (Pennsylvania), US (United States of America)
Williams, William V., Havertown, PA (Pennsylvania), US (United States of America)
Wang, Bin, Havertown, PA (Pennsylvania), US (United States of America)
ASSIGNEE(s): The Trustees of the University of Pennsylvania, (A U.S. Company or Corporation), Philadelphia, PA (Pennsylvania), US (United States of America)
The Wistar Institute, (A U.S. Company or Corporation), Philadelphia, PA (Pennsylvania), US (United States of America)
[Assignee Code(s): 64664; 92890]
APPL. NO.: 8-783,818
FILED: January 13, 1997 (19970113)

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a Continuation application of U.S. patent application Ser. No. 08-125,012 filed Sep. 21, 1993, which issued as U.S. Pat. No. 5,593,972 on Jan. 14, 1997, which is a Continuation-In-Part application of U.S. patent application Ser. No. 08-029,336 filed Mar. 11, 1993, abandoned; which is a Continuation-In-Part application of U.S. patent application Ser. No. 08-008,342 filed Jan. 26, 1993, abandoned; all of which are incorporated herein by reference.

FULL TEXT: 3529 lines

ABSTRACT

Methods of prophylactic and therapeutic immunization of an individual against pathogen infection, diseases associated with hyperproliferative cells and autoimmune diseases are disclosed. The methods comprise the steps of administering to cells of an individual, a nucleic acid molecule that comprises a nucleotide sequence that encodes a protein which comprises at least one epitope that is identical or substantially similar to an epitope of a pathogen antigen, a hyperproliferative cell associated protein or a protein associated with autoimmune disease respectively. In each case, nucleotide sequence is operably linked to regulatory sequences to enable expression in the cells. The nucleic acid molecule is free of viral particles and capable of being expressed in said cells. The cells may be contacted cells with a cell stimulating agent. Methods of prophylactically and therapeutically immunizing an individual against HIV are disclosed. Pharmaceutical compositions and kits for practicing methods of the present invention are disclosed.

02732313
Utility
GENE THERAPY FOR T CELL REGULATION
[Anticarcinogenic agents using liposomes and genetic engineering]

PATENT NO.: 5,705,151
ISSUED: January 06, 1998 (19980106)
INVENTOR(s): Dow, Steve W., Denver, CO (Colorado), US (United States of America)
Elmslie, Robyn E., Denver, CO (Colorado), US (United States of America)
ASSIGNEE(s): National Jewish Center for Immunology & Respiratory Medicine, (A U.S. Company or Corporation), Denver, CO (Colorado), US (United States of America)
[Assignee Code(s): 20719]
APPL. NO.: 8-446,918
FILED: May 18, 1995 (19950518)

This invention was made in part with government support AI00952-05, awarded by the National Institutes of Health. The government has certain rights to this invention.

FULL TEXT: 2286 lines

ABSTRACT

The present invention provides a nucleic acid-based therapeutic composition to treat an animal with disease by controlling the activity of effector cells, including T cells, macrophages, monocytes and/or natural killer cells, in the animal. The present invention also relates to methods of gene therapy involving different modes of administration of a therapeutic composition to treat animals with different types of diseases. Also included in the present invention are recombinant molecules for use in a therapeutic composition and recombinant cells useful as a **tumor vaccine**. Therapeutic compositions of the present invention include superantigen-encoding nucleic acid molecules, either in the presence or absence of a cytokine-encoding nucleic acid molecule, depending upon the disease being treated.
?

22/3,AB/1 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01420533 Genuine Article#: GY047 Number of References: 44
Title: INFECTIOUS ENVELOPED RNA VIRUS ANTIGENIC CHIMERAS
Author(s): LONDON SD; SCHMALJOHN AL; DALRYMPLE JM; RICE CM
Corporate Source: WASHINGTON UNIV,SCH MED,DEPT MOLEC MICROBIOL,660 S EUCLID AVE,BOX 8230/ST LOUIS//MO/63110; WASHINGTON UNIV,SCH MED,DEPT MOLEC MICROBIOL,660 S EUCLID AVE,BOX 8230/ST LOUIS//MO/63110; USA,MED RES INST INFECT DIS/FREDERICK//MD/21702
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 1992, V89, N1 (JAN 1), P207-211
Language: ENGLISH Document Type: ARTICLE
Abstract: Random insertion mutagenesis has been used to construct infectious Sindbis virus structural protein chimeras containing a neutralization epitope from a heterologous virus, Rift Valley fever virus. Insertion sites, permissive for recovery of chimeric viruses with growth properties similar to the parental virus, were found in the virion **E2** glycoprotein and the secreted **E3** glycoprotein. For the **E2** chimeras, the epitope was expressed on the virion surface and stimulated a partially protective immune response to Rift Valley fever virus infection in vivo. Besides providing a possible approach for developing live **attenuated** vaccine viruses, insertion of peptide ligands into virion surface proteins may ultimately allow targeting of virus infection to specific cell types.

22/3,AB/4 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0196694 DBA Accession No.: 96-08074
A viral vaccine vector that expresses foreign genes in lymph nodes and protects against mucosal challenge- influenza virus hemagglutinin gene expression in mouse using Venezuelan equine encephalitis virus **replication-competent** vector, **for use as a live, replication-competent recombinant vaccine**
AUTHOR: Davis N L; Brown K W; +Johnston R E
CORPORATE AFFILIATE: Univ.North-Carolina
CORPORATE SOURCE: Department of Microbiology and Immunology, School of Medicine, University of North Carolina, Chapel Hill, NC 27599, USA.
JOURNAL: J.Virol. (70, 6, 3781-87) 1996
ISSN: 0022-538X CODEN: JOVIAM
LANGUAGE: English
ABSTRACT: A candidate live-virus vaccine strain of Venezuelan-horse-encephalitis virus (VEE) was used as a replication-competent vector for in vivo expression of heterologous immunogens. A representative vaccine candidate, V3014, containing 2 **attenuating** mutations (**E2** (Lys-209) and **E2** (Thr-272)) was converted to a replication-competent VEE vaccine vector by placing a second copy of the 26S subgenomic RNA promoter and a unique ClaI site at the exact 3' end of the structural gene region). To test the vector for its ability to express a heterologous gene, the cloned influenza virus hemagglutinin (HA) gene from strain PR/8/34 was introduced at the unique ClaI site downstream of the 2nd subgenomic promoter. VEE vector virus without an insert, HA vector virus, and AH vector virus (containing the HA gene in non-coding orientation) were produced by transfection of BHK cells with in vitro synthesized RNA transcripts of the appropriate cDNA clones. After s.c. inoculation into the footpad of mice, the VEE vector containing the complete HA gene, expressed HA in

the draining lymph node and induced anti-HA inoculation. (39 ref)

22/3,AB/6 (Item 2 from file: 348)
DIALOG(R)File 348:European Patents

00743872
Recombinant infectious non-segmented negative strand RNA virus
Rekombinantes infektioses nicht-in-Segmente-geteiltes, negativ-Strange-RNS-Virus
Virus ARN recombinant, infectieux, non-segmente, brin-negatif
PATENT ASSIGNEE:
Akzo Nobel N.V., (200754), Velperweg 76, NL-6824 BM Arnhem, (NL),
(applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Conzelmann, Karl Klaus, Ammerseestr.34, D-82061 Neuried, (DE)
LEGAL REPRESENTATIVE:
Vossius, Volker, Dr. et al (12524), Dr. Volker Vossius,
Patentanwaltskanzlei - Rechtsanwaltskanzlei, Holbeinstrasse 5, 81679 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 702085 A1 960320 (Basic)
APPLICATION (CC, No, Date): EP 95201936 950714;
PRIORITY (CC, No, Date): EP 94202089 940718
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/86; C12N-015/47; C07K-014/145; A61K-039/205; C07K-014/16; C07K-014/185;

ABSTRACT EP 702085 A1
The present invention provides the generation of infectious replicating non-segmented negative-stranded RNA virus, entirely from cloned cDNA. This process offers the possibility to introduce mutations into the virus genome by means of recombinant DNA techniques.
ABSTRACT WORD COUNT: 45

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	508
SPEC A	(English)	EPAB96	10323
Total word count - document A			10831
Total word count - document B			0
Total word count - documents A + B			10831

22/3,AB/9 (Item 3 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00402064
METHOD OF INDUCING AN IMMUNE RESPONSE WITH A LIVE VENEZUELAN EQUINE ENCEPHALITIS VIRUS EXPRESSING A HETEROLOGOUS IMMUNOGEN
PROCEDE D'INDUCTION DE REACTION IMMUNITAIRE AU MOYEN D'UN VIRUS VIVANT DE L'ENCEPHALITE EQUINE DE VENEZUELA EXPRIMANT UN IMMUNOGENE HETEROLOGUE
Patent Applicant/Assignee:
THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
Inventor(s):
JOHNSTON Robert E
DAVIS Nancy L

SMITH Jonathan F
GRIEDER Franziska B
Patent and Priority Information (Country, Number, Date):
Patent: WO 9532733 A1 19951207
Application: WO 95US6739 19950526 (PCT/WO US9506739)
Priority Application: US 94250445 19940527
Designated States: AU CA HU JP KR MX NZ AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 5087
English Abstract

A method of protecting a subject against a disease comprises adminstering a recombinant Venezuelan Equine Encephalitis (VEE) Virus to the subject in an effective immunogenic amount, with the VEE virus containing a heterologous RNA segment, and with the heterologous segment comprising a promoter operable in the subject operatively associated with a sequence encoding an immunogenic protein or peptide effective for protecting the subject from the disease. Preferred promoters are VEE 26S subgenomic promoters, and preferred immunogens are viral immunogens. Novel **attenuating** mutations useful in carrying out the invention are also disclosed.

French Abstract

Le procede de la presente invention permet la protection d'un sujet contre une affection. Il consiste a administrer au sujet une qqantite immunogeniquement efficace de virus de l'encephalite equine du Venezuela contenant un segment d'ARN heterologue, lequel comporte un promoteur fonctionnel dans le sujet et fonctionnellement associe a une sequence codant une proteine ou un peptide immunogene efficace pour proteger le sujet contre l'affection. Les promoteurs preferes sont les promoteurs sub-genomique 26S de l'encephalite equine du Venezuela, les immunogenes preferes etant les immunogenes viraux. L'invention concerne egalement de nouvelles mutations attenuantes permettant la mise en oeuvre de l'invention.

22/3,AB/10 (Item 4 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00300516
DNA EXPRESSION SYSTEMS BASED ON ALPHAVIRUSES
SYSTEMES D'EXPRESSION DE L'ADN BASES SUR LES ALPHAVIRUS
Patent Applicant/Assignee:
BIOPTION AB
GAROFF Henrik
LILJESTROM Peter
Inventor(s):
GAROFF Henrik
LILJESTROM Peter
Patent and Priority Information (Country, Number, Date):
Patent: WO 9210578 A1 19920625
Application: WO 91SE855 19911212 (PCT/WO SE9100855)
Priority Application: SE 903978 19901213
Designated States: AT AT AU BB BE BF BG BJ BR CA CF CG CH CH CI CM DE DE DK DK ES ES FI FR GB GN GR HU IT JP KP KR LK LU LU MC MG ML MR MW NL NL NO PL RO SD SE SE TD TG US
Publication Language: English
Fulltext Word Count: 15628

English Abstract

Efficient protein production from cloned DNA in animal cells has been hampered by the lack of suitable expression systems. The requirements of such an expression system are (1) to produce functional or immunogenic forms of protein molecules in a wide variety of animal cells, (2) high efficiency and (3) technical simplicity. The present invention is related to a technical solution to this problem. A DNA molecule encoding protein sequences is inserted into engineered variants of the cDNA of a positive stranded RNA virus genome from alphavirus which then, via RNA transcription and transfection into tissue culture cells, is used to produce either chimaeric virus particles for immunization or recombinant virus for protein production. Because of optimized conditions of transfection and the nature of the virus replication the present system combines both simplicity and safety in terms of handling, efficiency in terms of level of protein and RNA production, as well as broad host range.

French Abstract

Le manque de sytemes d'expression appropries a empeche la production efficace de proteines a partir de l'ADN clone de cellules animales. Les exigences d'un tel systeme d'expression sont (1) de produire des formes fonctionnelles ou immunogenes de molecules de proteines dans une variete importante de cellules animales, (2) une efficacite elevee et (3) une simplicite technique. L'invention apporte une solution technique a ce probleme. On insere une molecule d'ADN codant des sequences de proteines dans des variantes produites par ingenierie de l'ADNc d'un genome de virus a ARN positif provenant d'un alphavirus, qu'on utilise, au moyen d'une transcription et d'une transfection d'ARN dans des cellules de culture tissulaires, pour produire soit des particules de virus chimeriques servant a l'immunisation, soit des virus recombinants servant a la production de proteines. Grace aux conditions optimisees de la transfection et a la nature de la replication du virus, ce systeme combine a la fois la simplicite et la securite en termes de manipulation, d'efficacite en termes de niveau de production de proteines et d'ARN, ainsi qu'une serie d'hotes importante.

22/3,AB/12 (Item 2 from file: 654)

02846593

Utility

SYSTEM FOR THE IN VIVO DELIVERY AND EXPRESSION OF HETEROLOGOUS GENES IN THE BONE MARROW

[Using **alphaviruses** as **vectors** containing immunogenic or therapeutic proteins;]

PATENT NO.: 5,811,407
ISSUED: September 22, 1998 (19980922)
INVENTOR(s): Johnston, Robert E., Chapel Hill, NC (North Carolina), US (United States of America)
Davis, Nancy L., Chapel Hill, NC (North Carolina), US (United States of America)
Simpson, Dennis A., Pittsboro, NC (North Carolina), US (United States of America)
ASSIGNEE(s): The University of North Carolina at Chapel Hill, (A U.S. Company or Corporation), Chapel Hill, NC (North Carolina), US (United States of America)
[Assignee Code(s): 5583]
APPL. NO.: 8-801,263
FILED: February 19, 1997 (19970219)

FEDERALLY SPONSORED RESEARCH

This invention was made with Government support under Grant Number 5 RO1 AI22186 from the National Institutes of Health. The Government has certain rights to this invention.

FULL TEXT: 4422 lines

ABSTRACT

The present invention provides a method of delivering immunogenic or therapeutic proteins to bone marrow cells using **alphavirus vectors** . The **alphavirus vectors** disclosed herein target specifically to bone marrow tissue, and viral genomes persist in bone marrow for at least three months post-infection. No or very low levels of virus were detected in quadricep, brain, and sera of treated animals. The sequence of a consensus Sindbis cDNA clone, pTR339, and infectious RNA transcripts, infectious virus particles, and pharmaceutical formulations derived therefrom are also disclosed. The sequence of the genomic RNA of the Girdwood S.A. virus, and cDNA clones, infectious RNA transcripts, infectious virus particles, and pharmaceutical formulations derived therefrom are also disclosed.

22/3,AB/16 (Item 6 from file: 654)

02663032

Utility

METHOD OF INDUCING AN IMMUNE RESPONSE WITH A LIVE VENEZUELAN EQUINE ENCEPHALITIS VIRUS EXPRESSING A HETEROLOGOUS IMMUNOGEN

PATENT NO.: 5,643,576
ISSUED: July 01, 1997 (19970701)
INVENTOR(s): Johnston, Robert E., Chapel Hill, NC (North Carolina), US (United States of America)
Davis, Nancy L., Chapel Hill, NC (North Carolina), US (United States of America)
Smith, Jonathan F., Sabillasville, MD (Maryland), US (United States of America)
Grieder, Franziska B., Bethesda, MD (Maryland), US (United States of America)
ASSIGNEE(s): The University of North Carolina at Chapel Hill, (A U.S. Company or Corporation), Chapel Hill, NC (North Carolina), US (United States of America)
[Assignee Code(s): 5583]
APPL. NO.: 8-444,563
FILED: May 19, 1995 (19950519)

This application is a divisional of prior application Ser. No. 08-250,445, filed May 27, 1994, now issued as U.S. Pat. No. 5,505,947, the disclosure of which is incorporated by reference herein in its entirety.

This invention was made with Government support under grant number DAMD17-91-C-1092 from the U.S. Army and grant number 5 RO1 N 526681-05 from the National Institutes of Health. The Government has certain rights to this invention.

FULL TEXT: 504 lines

ABSTRACT

A method of protecting a subject against a disease comprises administering a recombinant Venezuelan Equine Encephalitis (VEE) virus to the subject in an effective immunogenic amount, with the VEE virus containing a heterologous DNA segment, and with the heterologous DNA segment comprising a promoter operable in the subject operatively associated with a DNA encoding an immunogenic protein or peptide effective for protecting the subject from the disease. Preferred promoters are VEE 26S subgenomic promoters, and preferred immunogens are viral immunogens. Novel **attenuating** mutations useful in carrying out the invention are also disclosed.

22/3,AB/18 (Item 8 from file: 654)
DIALOG(R)File 654:US Pat.Full.

02514156
Utility
ATTENUATING MUTATIONS IN VENEZUELAN EQUINE ENCEPHALITIS VIRUS
[Live **attenuated** vaccines]

PATENT NO.: 5,505,947
ISSUED: April 09, 1996 (19960409)
INVENTOR(s): Johnston, Robert E., Chapel Hill, NC (North Carolina), US (United States of America)
Davis, Nancy L., Chapel Hill, NC (North Carolina), US (United States of America)
Smith, Jonathan F., Sabillasville, MD (Maryland), US (United States of America)
Grieder, Franziska B., Bethesda, MD (Maryland), US (United States of America)
ASSIGNEE(s): The University of North Carolina at Chapel Hill, (A U.S. Company or Corporation), Chapel Hill, NC (North Carolina), US (United States of America)
[Assignee Code(s): 5583]
EXTRA INFO: Assignment transaction [Reassigned], recorded July 26, 1999 (19990726)
APPL. NO.: 8-250,445
FILED: May 27, 1994 (19940527)

FULL TEXT: 457 lines

ABSTRACT

Novel **attenuating** mutations of Venezuelan Equine Encephalitis (VEE) are disclosed. Further aspects of the invention include an infectious VEE virus transcript encoded by cDNA clones, infectious VEE virus particles, and pharmaceutical formulations containing such infectious particles. Also disclosed are recombinant VEE virus containing a heterologous RNA segment.
?

29/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:European Patents

00510152
MULTIPLE PROMOTER BACULOVIRUS EXPRESSION SYSTEM AND DEFECTIVE PARTICLE PRODUCTION.
MIT MEHREREN PROMOTOREN BAKULOVIRENEXPRIMIERUNGSSYSTEM UND HERSTELLUNG VON DEFEKTIVEN PARTIKELN.
SYSTEME D'EXPRESSION DE BACULOVIRUS A PROMOTEURS MULTIPLES ET PRODUCTION DE PARTICULES DEFECTIVES.
PATENT ASSIGNEE:
THE TEXAS A & M UNIVERSITY SYSTEM, (421773), 308 WERC Building, College Station, TX 77843, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
OKER-BLOM, Christian, E., G. 30 Akademi, Universtiy Department of Biochemistry and Pharmacy, Porthansgatan 3 SF-20500 Turku, (FI)
SUMMERS, Max, D., 1908 Streamside Way, Bryan, TX 77801, (US)
LEGAL REPRESENTATIVE:
Dost, Wolfgang, Dr.rer.nat.,Dipl.-Chem. et al (3042), Patent- und Rechtsanwalte, Bardehle . Pagenberg . Dost . Altenburg . Frohwitter . Geissler & Partner, Postfach 86 06 20, D-81633 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 549721 A1 930707 (Basic)
EP 549721 B1 940413
WO 9205264 920402
APPLICATION (CC, No, Date): EP 91918840 910917; WO 91US6722 910917
PRIORITY (CC, No, Date): US 583392 900917
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/86; A61K-039/20; C12N-007/00; C12N-015/40;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	433
CLAIMS B	(German)	EPBBF1	419
CLAIMS B	(French)	EPBBF1	526
SPEC B	(English)	EPBBF1	12873
Total word count - document A			0
Total word count - document B			14251
Total word count - documents A + B			14251

29/3,AB/2 (Item 1 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00656436
PROTEINS ENCODED BY POLYNUCLEIC ACIDS OF PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME VIRUS (PRRSV)
PROTEINES CODEES PAR DES ACIDES POLYNUCLEIQUES DU VIRUS DU SYNDROME DYSGENESIQUE RESPIRATOIRE PORCIN (SDRP)
Patent Applicant/Assignee:
IOWA STATE UNIVERSITY RESEARCH FOUNDATION, IOWA STATE UNIVERSITY RESEARCH FOUNDATION , 310 Lab of Mechanics, Ames, IA 50011 , US
AMERICAN CYANAMID COMPANY, AMERICAN CYANAMID COMPANY , 5 Giralda Farms, Madison, NJ 07940 , US
Inventor(s):

PAUL Prem S, PAUL, Prem, S. , 4206 Arizona Circle, Ames, IA 50014 , US
ZHANG Yanjin, ZHANG, Yanjin , 2626 Babcock &2201, San Antonio, TX 78229 , US
Patent and Priority Information (Country, Number, Date):
Patent: WO 9939582 A1 19990812
Application: WO 99US2630 19990208 (PCT/WO US9902630)
Priority Application: US 9819793 19980206
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
Publication Language: English
Filing Language: English
Fulltext Word Count: 35520

English Abstract
The present invention provides a purified preparation containing, for example, at least one polypeptide selected from the group consisting of proteins encoded by one or more open reading frames (ORF's) of an Iowa strain of porcine reproductive and respiratory syndrome virus (PRRSV), antigenic regions of such proteins which are at least 5 amino acids in length and which effectively protect a porcine host against a subsequent challenge with a PRRSV isolate, and combinations thereof in which amino acids non-essential for antigenicity may be conservatively substituted. The present invention also concerns a vaccine comprising an effective amount of such a protein; antibodies which specifically bind to such a protein; methods of producing the same; and methods of protecting a pig against a PRRSV, treating a pig infected by a PRRSV, and detecting PRRSV in a pig.
French Abstract
La presente invention concerne une preparation purifiee renfermant, par exemple, au moins un polypeptide selectionne dans le groupe constitue par des proteines codees par un ou plusieurs cadres de lectures (ORF) d'une souche Iowa du virus du syndrome dysgenesique respiratoire porcin (SDRP), des regions antigeniques de ces proteines comportant au moins 5 acides amines en longueur et protegeant efficacement un hote porcin contre une contamination ulterieure par un isolat du SDRP, ainsi que des combinaisons de celles-ci dans lesquelles les acides amines non essentiels a l'antigenicite peuvent etre raisonnablement substitues. Cette invention concerne par ailleurs un vaccin comprenant une dose efficace de cette proteine, des anticorps se fixant specifiquement sur cette proteine, des procedes de sa fabrication, ainsi que des procedes de protection d'un cochon contre le SDRP, le traitement d'un cochon infecte par le SDRP et la detection de ce syndrome chez un cochon.
?

36/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09387711 98096342
Replicon-helper systems from attenuated Venezuelan equine encephalitis virus: expression of heterologous genes in vitro and immunization against heterologous pathogens in vivo.
Pushko P; Parker M; Ludwig GV; Davis NL; Johnston RE; Smith JF
Virology Division, U.S. Army Medical Research Institute for Infectious Diseases, Fort Detrick, Frederick, Maryland 21702, USA.
Virology (UNITED STATES) Dec 22 1997, 239 (2) p389-401, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A replicon vaccine vector system was developed from an attenuated strain of **Venezuelan equine encephalitis virus** (VEE). The replicon RNA consists of the cis-acting 5' and 3' ends of the VEE genome, the complete nonstructural protein gene region, and the subgenomic 26S promoter. The genes encoding the VEE structural proteins were replaced with the **influenza** virus **hemagglutinin** (**HA**) or the Lassa virus nucleocapsid (N) gene, and upon transfection into eukaryotic cells by electroporation, these replicon RNAs directed the efficient, high-level synthesis of the **HA** or N proteins. For packaging of replicon RNAs into VEE replicon particles (VRP), the VEE capsid and glycoproteins were supplied in trans by expression from helper RNA(s) coelectroporated with the replicon. A number of different helper constructs, expressing the VEE structural proteins from a single or two separate helper RNAs, were derived from attenuated VEE strains Regeneration of infectious virus was not detected when replicons were packaged using a bipartite helper system encoding the VEE capsid protein and glycoproteins on two separate RNAs. Subcutaneous immunization of BALB/c mice with VRP expressing the **influenza HA** or Lassa virus N gene (**HA** -VRP or N-VRP, respectively) induced antibody responses to the expressed protein. After two inoculations of **HA** -VRP, complete protection against intranasal challenge with **influenza** was observed. Furthermore, sequential immunization of mice with two inoculations of N-VRP prior to two inoculations of **HA** -VRP induced an immune response to both **HA** and N equivalent to immunization with either VRP construct alone. Protection against **influenza** challenge was unaffected by previous N-VRP immunization. Therefore, the VEE replicon system was characterized by high-level expression of heterologous genes in cultured cells, little or no regeneration of plaque-forming virus particles, the capability for sequential immunization to multiple pathogens in the same host, and induction of protective immunity against a mucosal pathogen.

36/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08659425 96211511
A viral vaccine vector that expresses foreign genes in lymph nodes and protects against mucosal challenge.
Davis NL; Brown KW; Johnston RE
Department of Microbiology and Immunology, School of Medicine, University of North Carolina, Chapel Hill, 27599, USA.
Journal of virology (UNITED STATES) Jun 1996, 70 (6) p3781-7, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: AI22186, AI, NIAID; NS26681, NS, NINDS
Languages: ENGLISH

Document type: JOURNAL ARTICLE
A candidate live-virus vaccine strain of **Venezuelan equine encephalitis virus** (VEE) was configured as a replication-competent **vector** for in vivo expression of heterologous immunogens. Three features of VEE recommend it for use as a vaccine **vector** . (i) Most human and animal populations are not already immune to VEE, so preexisting immunity to the **vector** would not limit expression of the heterologous antigen. (ii) VEE replicates first in local lymphoid tissue, a site favoring the induction of an effective immune response. (iii) Parenteral immunization of rodents and humans with live, attenuated VEE vaccines protects against mucosal challenge, suggesting that VEE vaccine **vectors** might be used successfully to protect against mucosal pathogens. Upon subcutaneous (s.c.) inoculation into the footpad of mice, a VEE **vector** containing the complete **influenza** virus **hemagglutinin** (**HA**) gene expressed **HA** in the draining lymph node and induced anti-**HA** immunoglobulin G (IgG) and IgA serum antibodies, the levels of which could be increased by s.c. booster inoculation. When immunized mice were challenged intranasally with a virulent strain of **influenza** virus, replication of challenge virus in their lungs was restricted, and they were completely protected from signs of disease. Significant reduction of **influenza** virus replication in the nasal epithelia of **HA** **vector** -immunized mice suggested an effective immunity at the mucosal surface. VEE vaccine **vectors** represent an alternative vaccination strategy when killed or subunit vaccines are ineffective or when the use of a live attenuated vaccine might be unsafe.

36/3,AB/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09749777 BIOSIS NO.: 199598204695
Protection against influenza **in mice by vaccination with a** Venezuelan equine encephalitis virus vector **expressing the** HA **protein.**
AUTHOR: Davis Nancy L(a); Brown Kevin W(a); Caley Ian J(a); Swanstrom Ronald L; Johnston Robert E(a)
AUTHOR ADDRESS: (a)Dep. Microbiol. and Immunol., Univ. N.C., Chapel Hill, NC 27599**USA
1995
JOURNAL: Journal of Cellular Biochemistry Supplement 0 (19A):p310 1995
CONFERENCE/MEETING: Keystone Symposium on Molecular Aspects of Viral Immunity Keystone, Colorado, USA January 16-23, 1995
ISSN: 0733-1959
RECORD TYPE: Citation
LANGUAGE: English

36/3,AB/6 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0202638 DBA Accession No.: 96-13409
Attenuated Venezuelan equine encephalitis virus **vaccine** vectors **express immunogens of heterologous pathogens in vivo and induce mucosal immunity- attenuated Venezuelan-horse-encephalitis virus vector mutant for** influenza **virus** hemagglutinin **gene transfer and expression; application as recombinant vaccine (conference abstract)**
AUTHOR: Davis N L; Brown K W; Charles P C; Caley I J; Swanstrom R I; Smith J F; Johnston R E
CORPORATE AFFILIATE: Univ.North-Carolina U.S.Army-Res.Inst.Infec.Dis.
CORPORATE SOURCE: Department of Microbiology and Immunology, University f North Carolina, Chapel Hill, NC, USA.

JOURNAL: Am.J.Trop.Med.Hyg. (53, 2, Suppl., 112) 1995
ISSN: 0002-9637 CODEN: AJTHAB
CONFERENCE PROCEEDINGS: American Society of Tropical Medicine and Hygiene, 44th Annual Meeting, San Antonio, Texas, USA, on 17-21 November, 1995.
LANGUAGE: English
ABSTRACT: A mutant of Venezuelan-horse-encephalitis virus (VEE) was inoculated s.c. into mice and induced protective immunity against s.c. or intranasal (i.n.) challenge with virulent VEE. Effective mucosal immunity was demonstrated by the induction of VEE-specific IgA and complete protection of the nasal tissues of i.n. challenged mice from VEE infection. This attenuated cDNA clone was altered to contain a 2nd subgenomic RNA promoter and a complete **influenza** virus **hemagglutinin** (**HA**) gene immediately downstream of the structural gene region. The **HA** protein was expressed from the 2nd promoter. CD-1 mice were inoculated s.c. with 20,000 pfu of the **HA** vector. Expression of **HA** mRNA was detected in the draining lymph node of inoculated mice. Significant increases in titers occurred after administration of a booster immunization. After i.n. **influenza** challenge, 100% morbidity and 50% mortality were observed in controls, whereas morbidity/mortality were both 0% following the boost. These experiments demonstrate the feasibility of using vectors based on attenuated VEE cDNA clones to induce protective systemic and mucosal immunity against heterologous pathogens. (0 ref)

36/3,AB/7 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0191256 DBA Accession No.: 96-02027 PATENT
Immune protection of subjects from disease- Venezuelan- equine-encephalitis virus vector-**mediated immunogen e.g.** influenza **virus** hemagglutinin **surface protein expression for use in recombinant vaccine**
AUTHOR: Johnston R E; Davis N L; Smith J F; Grieder F B
CORPORATE SOURCE: Chapel Hill, NC, USA.
PATENT ASSIGNEE: Univ.North-Carolina 1995
PATENT NUMBER: WO 9532733 PATENT DATE: 951207 WPI ACCESSION NO.: 96-030338 (9603)
PRIORITY APPLIC. NO.: US 250445 APPLIC. DATE: 940527
NATIONAL APPLIC. NO.: WO 95US6739 APPLIC. DATE: 950526
LANGUAGE: English
ABSTRACT: A method of protecting a subject against disease is claimed, which involves administering a recombinant Venezuelan-equine-encephalit is (VEE) virus to the subject in an effective immunogenic amount, where the virus contains at least one attenuating mutation and a heterologous DNA segment (preferably at least 1 kb in length) containing a promoter operable in the subject operatively associated with DNA encoding an immunogen effective for protecting the subject from the disease. Also claimed are: (a) the DNA; (b) an infectious VEE virus RNA transcript encoded by the DNA; and (c) infectious VEE virus particles containing the RNA transcript. Preferred immunogens are those from the lenti virus, corona virus, flavi virus and **influenza** virus, especially the **influenza** virus **hemagglutinin** surface protein. The preferred promoter is the VEE virus 26S subgenomic promoter. Novel attenuating mutations are also disclosed. Advantageously, the heterologous insert can be relatively large (at least 1 kb in length). (32pp)

36/3,AB/9 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

123311767 CA: 123(23)311767v CONFERENCE PROCEEDING
An attenuated VEE virus vaccine vector: Expression of HIV-1 and influenza genes in cell culture and protection against influenza challenge in mice immunized with a vector expressing HA
AUTHOR(S): Davis, Nancy L.; Brown, Kevin W.; Caley, Ian; Charles, Peter C.; Swanstrom, Ronald; Johnston, Robert E.
LOCATION: School Medicine, University North Carolina, Chapel Hill, NC, 27599, USA
JOURNAL: Vaccines 95: Mol. Approaches Control Infect. Dis., (Annu. Meet.), 12th EDITOR: Chanock, Robert M (Ed), DATE: 1995 PAGES: 387-91
CODEN: 61TGAQ LANGUAGE: English MEETING DATE: 940000 PUBLISHER: Cold Spring Harbor Laboratory Press,Cold Spring Harbor, N. Y
?

48/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09695029 98375576
The labyrinthine ways of cancer **immunotherapy--T cell,** tumor **cell encounter: "how do I lose thee? Let me count the ways".**
Ellem KA; Schmidt CW; Li CL; Misko I; Kelso A; Sing G; **Macdonald G** ; O'Rourke MG
Queensland Cancer Fund Research Laboratories, Bancroft Centre, Brisbane, Australia.
Advances in cancer research (UNITED STATES) 1998, 75 p203-49, ISSN 0065-230X Journal Code: 2J6
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

48/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06013584 85145919
Role of etoposide-based chemotherapy in the treatment of patients with refractory or relapsing germ cell tumors.
Bosl GJ; Yagoda A; Golbey RB; Whitmore W Jr; Herr H; Sogani P; Morse M; Vogelzang N; **MacDonald G**
American journal of medicine (UNITED STATES) Mar 1985, 78 (3) p423-8, ISSN 0002-9343 Journal Code: 3JU
Contract/Grant No.: CA-05826, CA, NCI; N01-CM-07337, CM, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Forty-nine patients with metastatic germ cell tumors were treated with etoposide 100 mg/m2 and cisplatin 20 mg/m2 intravenously each day for five days as "salvage" chemotherapy. Forty-seven patients had received standard induction regimens for metastatic germ cell tumors before receiving etoposide and cisplatin. Four patients were treated after surgical resection of a single site of relapse (Group I). Forty-five patients had measurable or evaluable disease at the time of treatment. In 17 patients with evaluable disease who had either achieved a prior complete remission or received no prior cisplatin (Group II), eight (47 percent) complete and four (24 percent) partial remission were observed. In 28 patients who had never achieved a prior complete remission (Group III), no complete and five (18 percent) partial responses were observed. Seven of 21 patients in Groups I and II and none of 28 patients in Group III remain alive and free of disease. Assuming prior treatment with cisplatin-based chemotherapy, these data and a review of the published experience with similar salvage regimens for patients with relapsing or refractory germ cell tumors suggest that combination chemotherapy based on etoposide and cisplatin is effective primarily in those patients who achieved a prior complete remission. Such therapy is ineffective in the absence of a prior complete remission probably because the patients have tumors that are largely resistant to cisplatin. Observed responses are probably due to etoposide alone. Investigational therapies should be pursued in those patients whose disease is refractory to current induction regimens.

48/3,AB/13 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11025381 BIOSIS NO.: 199799646526

Major histocompatibility complex class II-transfected tumor **cells present endogenous antigen and are potent inducers of** tumor-**specific immunity.**
AUTHOR: Armstrong Todd D; Clements Virginia K; **Martin Brian K ; Ting Jenny P-Y** ; Ostrand-Rosenberg Suzanne(a
AUTHOR ADDRESS: (a)Dep. Biological Sci., Univ. Maryland Baltimore County, Baltimore, MD 21250**USA
1997
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 94 (13):p6886-6891 1997
ISSN: 0027-8424
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have developed an immunotherapy in which **tumor** cells transfected with syngeneic major histocompatibility complex (MHC) class II genes are cell-based **vaccines** for the treatment of established **tumor** and metastatic disease. If this strategy is to be used clinically, convenient methods for generating class II+ **tumor** cells are necessary. Interferon-gamma treatment or transduction of the class II transactivator (CIITA) gene induces class II expression but also up-regulates the class II-associated accessory molecules, invariant chain (Ii) and DM. To determine if interferon-gamma treatment and CIITA transduction are potential immunotherapies, we assessed the tumorigenicity of sarcoma cells expressing combinations of class II, Ii, and DM. Since we hypothesized that class II-transfected **tumor** cells not coexpressing Ii and DM present endogenously encoded **tumor** peptides, we have assessed the transfectants for antigen presentation activity to MHC class II-restricted antigen-specific CD4+ T cells. **Tumor** challenge studies demonstrate that **tumor** cells expressing class II without coexpression of Ii or Ii plus DM are highly **immunogenic** and preferentially present endogenous antigens, while tumors coexpressing class Ii with Ii or Ii plus DM are not effective immunogens. Because **tumor** rejection correlates with expression of class II without coexpression of Ii and DM, the most efficacious **vaccines** will express MHC class II without coexpression of Ii and DM and will preferentially present endogenous antigen.

48/3,AB/16 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09943481 BIOSIS NO.: 199598398399
Genetically engineered, live, attenuated vaccines **for Venezuelan equine encephalitis: Testing in nonhuman primates.**
BOOK TITLE: The 9th International Congress of Immunology
AUTHOR: Pratt W D(a); Davis N L; **Johnston R E** ; Smith J F(a
BOOK AUTHOR/EDITOR: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY
AUTHOR ADDRESS: (a)U.S.A.M.R.I.I.D., Ft. Detrick, Frederick, MD**USA
1995
p590 1995
BOOK PUBLISHER: 9th International Congress of Immunology, San Francisco, California, USA
CONFERENCE/MEETING: Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies San Francisco, California, USA July 23-29, 1995
RECORD TYPE: Citation
LANGUAGE: English

48/3,AB/17 (Item 13 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

09812049 BIOSIS NO.: 199598266967
Coordinate regulation of the human TAP1 and LMP2 genes from a shared bidirectional promoter.
AUTHOR: Wright Kenneth L; White Leigh C; Kelly Adrian; Beck Stephan; Trowsdale John; **Ting Jenny P-Y** (a
AUTHOR ADDRESS: (a)UNC Lineberger Comprehensive Cancer Cent., Dep. Microbiol.-Immunol., CB 7295, Univ. North Caroli**USA
1995
JOURNAL: Journal of Experimental Medicine 181 (4):p1459-1471 1995
ISSN: 0022-1007
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recently, four genes (TAP1, TAP2, LMP2, LMP7) involved or potentially involved in the processing and transport of major histocompatibility complex class I-associated antigen to the endoplasmic reticulum have been identified. We now report the initial characterization of the bidirectional promoter for the human transporter associated with antigen processing 1 (TAP1) and low molecular mass polypeptide 2 (LMP2) genes. These genes are divergently transcribed from a central promoter region of only 593 bp. Functional analysis using a bidirectional reporter system demonstrates the minimal 593-bp promoter is sufficient for concurrent expression in both directions. There is no TATA box homology at either end but there is a prevalence of GC boxes. Transcription is initiated at multiple sites for each gene without any of the TAP1 transcripts overlapping with the LMP2 transcripts. The region proximal to the TAP1 gene is required for maximal basal level expression of not only TAP1 but also LMP2. Furthermore, this region is necessary for **tumor** necrosis factor alpha (TNF-alpha) induction of both genes. Site-specific mutations of an NF-kappa-B element in the TAP1 proximal region blocked induction by TNF-alpha in both the TAP1 and LMP2 directions. An adjacent GC box was required for basal expression of both genes as well as augmenting the TNF-alpha induction of the distal LMP2 gene. In vivo genomic foot-printing of this region revealed strong protein/DNA interactions at the NF-kappa-B and GC box consensus sequences. In vitro binding studies confirmed the capacity of the NF-kappa-B site to bind p50/p65 and p52/p65 heterodimers and of the GC box to bind Sp1. Thus, the promoter elements proximal to the TAP1 gene play a significant role in regulating basal and induced expression of both TAP1 and LMP2. The findings presented in this report clearly link LMP2 expression with TAP1 expression and provide additional suggestive evidence linking LMP2 to class I antigen presentation.

48/3,AB/24 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07727478 BIOSIS NO.: 000092052109
ATTENUATING MUTATIONS IN THE E2 GLYCOPROTEIN GENE OF VENEZUELAN EQUINE ENCEPHALITIS VIRUS CONSTRUCTION OF SINGLE AND MULTIPLE MUTANTS IN A FULL-LENGTH COMPLEMENTARY DNA CLONE
AUTHOR: DAVIS N L; POWELL N; GREENWALD G F; WILLIS L V; JOHNSON B J B; SMITH J F; **JOHNSTON R E**
AUTHOR ADDRESS: DEP. MICROBIOL. IMMUNOL., SCH. MED., UNIV. NORTH CAROLINA, CHAPEL HILL, N.C. 27599.
JOURNAL: VIROLOGY 183 (1). 1991. 20-31.

FULL JOURNAL NAME: Virology
CODEN: VIRLA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Attenuated mutants of Venezuelan equine encephalitis (VEE) were isolated by selection for rapid penetration of cultured cells (R. E. Johnston and J. F. Smith, 1988, Virology 162, 437-443). Sequence analysis of these mutants identified candidate attenuating mutations at four loci in the VEE E2 glycoprotein gene: a double mutation at E2 codons 3 and 4, and single substitutions at E2 76, 120, and 209. Each candidate mutation was reproduced in an isogenic recombinant VEE strain site-directed mutagenesis of a full-length cDNA clone of VEE. Characterization of these molecularly cloned mutant viruses showed that mutation at each of the four loci in the E2 gene was sufficient to confer both the accelerated penetration and attenuation phenotypes. Inoculation of the molecularly cloned viruses into rodent models that differ in their response to VEE suggested that individual mutations affected different aspects of VEE pathogenesis. Full-length clones containing multiple mutations were produced by combining independently attenuatining mutations. Molecularly cloned viruses carrying two or three mutations were more attenuated in sensitive animal models than viruses which contained any single mutation alone. However, these highly attenuated strains still retained the ability to induce an immune response sufficient to protect against a high dose challenge with virulent VEE. These results indicate that production of a molecularly cloned live virus **vaccine** for VEE is feasible.

48/3,AB/26 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07320784 BIOSIS NO.: 000090100684
ATTENUATING MUTATIONS IN GLYCOPROTEINS E1 AND E2 OF SINDBIS VIRUS PRODUCE A HIGHLY ATTENUATED STRAIN WHEN COMBINED IN-VITRO
AUTHOR: POLO J M; **JOHNSTON R E**
AUTHOR ADDRESS: DEP. MICROBIOL. IMMUNOL., UNIV. NORTH CAROLINA, CHAPEL HILL, N.C. 27599.
JOURNAL: J VIROL 64 (9). 1990. 4438-4444.
FULL JOURNAL NAME: Journal of Virology
CODEN: JOVIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Alterations in either the E1 or the E2 glycoprotein of Sindbis virus can affect pathogenesis in animals. Previously, we identified two distinct E1 glycoprotein gene sequences which differed in their effect on pathogenesis. One had an attenuation phenotype following subcutaneous inoculation of neonatal mice (E1 Ala-72, Gly-75, and Ser-237), while the other was virulent (E1 Val-72, Asp-75, and Ala-237). In this study, we examined the basis for this difference in pathogenesis by using a full-length cDNA clone of Sindbus virus from which infectious RNA could be transcribed in vitro. The relative contribution of each E1 residue to the pathogenesis phenotype was determined by using site-directed mutagenesis to alter each codon individually and in combination. Residues 75 and 237, in combination, appeared to be the major E1 determinants affecting pathogenesis. In addition, the effect of directly combining independently attenuating E1 and E2 mutations in the same virus was examined. The attenuating E1 sequences characterized in this study were coupled to a previously characterized attenuating mutation at E2 residue 114. The resulting recombinant virus, constructed in vitro, exhibited an

increased attenuation of neurovirulence as compared with recombinant viruses containing either of the attenuating elements alone.

48/3,AB/27 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07195191 BIOSIS NO.: 000039109545
IN-VITRO SYNTHESIS OF INFECTIOUS VENEZUELAN EQUINE ENCEPHALITIS VIRUS RNA FROM A COMPLEMENTARY DNA CLONE ANALYSIS OF A VIABLE DELETION MUTANT AND MUTATIONS AFFECTING VIRULENCE
AUTHOR: DAVIS N L; WILLIS L V; GREENWALD G G; **JOHNSTON R E** ; SMITH J F
AUTHOR ADDRESS: DEP. MICROBIOL. IMMUNOL., UNIV. NORTH CAROLINA, CHAPEL HILL, N.C. 27599-7290.
JOURNAL: BROWN, F., ET AL. (ED.). VACCINES (COLD SPRING HARBOR), 90. MODERN APPROACHES TO NEW VACCINES INCLUDING PREVENTION OF AIDS; SEVENTH MEETING, SEPTEMBER 1989. XXV+502P. COLD SPRING HARBOR LABORATORY PRESS: COLD SPRING HARBOR, NEW YORK, USA. ILLUS. PAPER. ISBN 0-87969-341-X. 0 (0). 1990. 109-114.
CODEN: VMAVE
RECORD TYPE: Citation
LANGUAGE: ENGLISH

48/3,AB/28 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07195190 BIOSIS NO.: 000039109544
A MODEL FOR IN-VITRO DEVELOPMENT OF LIVE RECOMBINANT ALPHAVIRUS VACCINES
AUTHOR: POLO J M; **JOHNSTON R E**
AUTHOR ADDRESS: DEP. MICROBIOL. IMMUNOL., UNIV. NORTH CAROLINA, CHAPEL HILL, N.C., 27599-7920.
JOURNAL: BROWN, F., ET AL. (ED.). VACCINES (COLD SPRING HARBOR), 90. MODERN APPROACHES TO NEW VACCINES INCLUDING PREVENTION OF AIDS; SEVENTH MEETING, SEPTEMBER 1989. XXV+502P. COLD SPRING HARBOR LABORATORY PRESS: COLD SPRING HARBOR, NEW YORK, USA. ILLUS. PAPER. ISBN 0-87969-341-X. 0 (0). 1990. 105-108.
CODEN: VMAVE
RECORD TYPE: Citation
LANGUAGE: ENGLISH

48/3,AB/42 (Item 8 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

00816038 1998050687
Replicon-helper systems from attenuated Venezuelan equine encephalitis virus: Expression of heterologous genes in vitro and immunization against heterologous pathogens in vivo
Pushko P.; Parker M.; Ludwig G.V.; Davis N.L.; **Johnston R.E.** ; Smith J.F.
ADDRESS: J.F. Smith, Virology Division, US Army Med. Res. Inst. Infect. Dis., Fort Detrick, Frederick, MD 21702, United States
Journal: Virology, 239/2 (389-401), 1997, United States
PUBLICATION DATE: December 22, 1997
CODEN: VIRLA
ISSN: 0042-6822
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English

NO. OF REFERENCES: 53

A replicon **vaccine** vector system was developed from an attenuated strain of **Venezuelan equine encephalitis virus** (VEE). The replicon RNA consists of the cis-acting 5' and 3' ends of the VEE genome, the complete nonstructural protein gene region, and the subgenomic 26S promoter. The genes encoding the VEE structural proteins were replaced with the influenza virus hemagglutinin (HA) or the Lassa virus nucleocapsid (N) gene, and upon transfection into eukaryotic cells by electroporation, these replicon RNAs directed the efficient, high-level synthesis of the HA or N proteins. For packaging of replicon RNAs into VEE replicon particles (VRP), the VEE capsid and glycoproteins were supplied in trans by expression from helper RNA(s) coelectroporated with the replicon. A number of different helper constructs, expressing the VEE structural proteins from a single or two separate helper RNAs, were derived from attenuated VEE strains. Regeneration of infectious virus was not detected when replicons were packaged using a bipartite helper system encoding the VEE capsid protein and glycoproteins on two separate RNAs. Subcutaneous immunization of BALB/c mice with VRP expressing the influenza HA or Lassa virus N gene (HA-VRP or N-VRP, respectively) induced antibody responses to the expressed protein. After two inoculations of HA- VRP, complete protection against intranasal challenge with influenza was observed. Furthermore, sequential immunization of mice with two inoculations of N-VRP prior to two inoculations of HA-VRP induced an immune response to both HA and N equivalent to immunization with either VRP construct alone. Protection against influenza challenge was unaffected by previous N-VRP immunization. Therefore, the VEE replicon system was characterized by high- level expression of heterologous genes in cultured cells, little or no regeneration of plaque-forming virus particles, the capability for sequential immunization to multiple pathogens in the same host, and induction of protective immunity against a mucosal pathogen.

48/3,AB/44 (Item 10 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

00625310 97131980
Mucosal immunity induced by parenteral immunization with a live attenuated Venezuelan equine encephalitis virus vaccine **candidate**
Charles P.C.; Brown K.W.; Davis N.L.; Hart M.K.; **Johnston R.E.**
ADDRESS: P.C. Charles, Department of Pathology, Albert Einstein College of Medicine, 1300 Morris Park Ave, Bronx, NY 10461, United States
Journal: Virology, 228/2 (153-160), 1997, United States
PUBLICATION DATE: 19970000
CODEN: VIRLA
ISSN: 0042-6822
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 25

Induction of a mucosal immune response is generally thought to require introduction of an immunogen directly onto the mucosal surface. It has been observed, however, that live, attenuated mutants of the alphavirus, Venezuelan equine encephalitis virus (VEE), induce protection from virulent challenge at the respiratory mucosa even after parenteral inoculation. In this report, we propose a mechanism by which subcutaneous immunization with a molecularly cloned, attenuated double mutant of VEE is able to stimulate the production of mucosal anti-VEE IgA. Our results showed that the immunizing virus spread to, and replicated within, lymphoid tissues throughout the mouse. Several tissues known to be inductive sites of the

mucosal immune system were found to be positive for the presence of VEE RNA by 48 hr postimmunization. Moreover, this mucosal lymphotropism resulted in the production of virus-specific IgA antibody detectable in vaginal secretions of immunized mice.

48/3,AB/45 (Item 11 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

00566004 97068470
Humoral, mucosal, and cellular immunity in response to a human immunodeficiency virus type 1 immunogen expressed by a Venezuelan equine encephalitis virus vaccine vector
Caley I.J.; Betts M.R.; Irlbeck D.M.; Davis N.L.; Swanstrom R.; Frelinger J.A.; **Johnston R.E.**
ADDRESS: R.E. Johnston, Dept. of Microbiology and Immunology, School of Medicine, University of North Carolina, Chapel Hill, NC 27599, United States
Journal: Journal of Virology, 71/4 (3031-3038), 1997, United States
PUBLICATION DATE: 19970000
CODEN: JOVIA
ISSN: 0022-538X
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 54

A molecularly cloned attenuated strain of **Venezuelan equine encephalitis virus** (VEE) has been genetically configured as a replication-competent **vaccine vector** for the expression of heterologous viral proteins (N. L. Davis, K. W. Brown, and R. E. Johnston, J. Virol. 70:3781-3787, 1996). The matrix/capsid (MA/CA) coding domain of human immunodeficiency virus type 1 (HIV-1) was cloned into the VEE **vector** to determine the ability of a VEE **vector** to stimulate an anti-HIV immune response in mice. The VEE-MA/CA **vector** replicated rapidly in the cytoplasm of baby hamster kidney (BHK) cells and expressed large quantities of antigenically identifiable MA/CA protein. When injected subcutaneously into BALB/c mice, the **vector** invaded and replicated in the draining lymphoid tissues, expressing HIV-1 MA/CA at a site of potent immune activity. Anti-MA/CA immunoglobulin G (IgG) and IgA antibodies were present in serum of all immunized mice, and titers increased after a second booster inoculation. IgA antibodies specific for MA/CA were detected in vaginal washes of mice that received two subcutaneous immunizations. Cytotoxic T-lymphocyte responses specific for MA/CA were detected following immunization with the MA/CA-expressing VEE **vector** . These findings demonstrate the ability of a VEE-based **vaccine vector** system to stimulate a comprehensive humoral and cellular immune response. The multifaceted nature of this response makes VEE an attractive **vaccine** for immunization against virus infections such as HIV-1, for which the correlates of protective immunity remain unclear, but may include multiple components of the immune system.

48/3,AB/47 (Item 13 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

00386392 96079558
A viral vaccine **vector that expresses foreign genes in lymph nodes and protects against mucosal challenge**
Davis N.L.; Brown K.W.; **Johnston R.E.**

ADDRESS: R.E. Johnston, United States
Journal: Journal of Virology, 70/6 (3781-3787), 1996
PUBLICATION DATE: 19960000
CODEN: JOVIA
ISSN: 0022-538X
DOCUMENT TYPE: Article
LANGUAGES: English

48/3,AB/48 (Item 14 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

00314300 95127204
Attenuated mutants of Venezuelan equine encephalitis virus containing lethal mutations in the PE2 cleavage signal combined with a second-site suppressor mutation in E1
Davis N.L.; Brown K.W.; Greenwald G.F.; Zajac A.J.; Zacny V.L.; Smith J.F.; **Johnston R.E.**
ADDRESS: N.L. Davis, Dept. Microbioiogy and Immunology, University of North Carolina, Box 7290, Chapel Hill, NC 27599, United States
Journal: Virology, 212/1 (102-110), 1995, United States
PUBLICATION DATE: 19950000
CODEN: VIRLA
ISSN: 0042-6822
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English

The PE2 cleavage signal in a full-length cDNA clone of the alphavirus Venezuelan equine encephalitis virus (VEE) was ablated by site-directed mutagenesis. RNA transcripts derived from the resulting plasmids programmed the production of nonviable particles upon transfection of baby hamster kidney (BHK) cells. However, the mutant RNAs also gave rise to a small proportion of viable revertants. Analysis of these biological revertants and their molecularly cloned homologs demonstrated that second-site suppressor mutations at either E2 position 243 or E1 position 253 were able to restore viability to PE2 cleavage signal mutants. The viable revertants incorporated unprocessed PE2 into particles which showed normal infectivity for BHK cells, but reduced ability to grow in C6/36 mosquito cells. A mutant carrying a lethal PE2 cleavage signal mutation in combination with a suppressor at E1 253 was either avirulent or highly attenuated in adult mice when inoculated by the subcutaneous, intracerebral, or intranasal route and conferred complete protection against both intraperitoneal and intranasal challenge with virulent VEE. These results indicate the close functional association of the E2 and E1 proteins in the alphavirus spike. They also have implications for the design of recombinant live virus **vaccines** for VEE, for other alphaviruses, and for other viruses that use a similar mechanism for glycoprotein maturation.

48/3,AB/53 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0247206 DBA Accession No.: 2000-01696 PATENT
A composition for modifying mammalian cells, useful for stimulating immune response in cancer **patients- alpha virus or Venezuelan-horse-encephalitis virus-mediated** cancer **antigen expression in** cancer **cell for** vaccine
AUTHOR: **MacDonald G H ; Martin B K ; Johnston R E ;** Ting J P Y
CORPORATE SOURCE: Chapel Hill, NC, USA.

PATENT ASSIGNEE: Univ.North-Carolina 1999
PATENT NUMBER: WO 9951263 PATENT DATE: 19991014 WPI ACCESSION NO.: 2000-013031 (2001)
PRIORITY APPLIC. NO.: US 81092 APPLIC. DATE: 19980408
NATIONAL APPLIC. NO.: WO 99US7704 APPLIC. DATE: 19990408
LANGUAGE: English
ABSTRACT: A composition containing alpha virus particles, preferably an alpha virus replicon particle or a Venezuelan-horse-encephalitis virus, is new. The alpha virus particles contain at least one heterologous nucleotide sequence encoding an antigen. The antigen is selected from a native sequence encoding an antigen. The antigen is selected from a native **cancer** cell antigen and an artificial **cancer** antigen that is not normally expressed by a **cancer** cell. Also claimed are: a pharmaceutical formulation containing the composition and a carrier; a kit for modifying a mammalian cell including a vector for introducing and expressing an antigen in a mammalian cell; a method for inducing a protective immune response in a subject afflicted with **cancer** ; and a method for inducing a protective immune response in a subject afflicted with **cancer** . The composition is useful for the stimulation of a protective immune response in **cancer** patients. (46pp)

48/3,AB/57 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0205660 DBA Accession No.: 97-00781
Development of a generic vaccine **delivery system based on a Venezuelan-equine-encephalitis (VEE) virus replicon-Venezuelan-horse-encephalitis virus vector attenuation for recombinant** vaccine **construction (conference abstract)**
AUTHOR: Pushko P; Parker M; Ludwig G V; Davis N L; **Johnston R E** ; Smith J F
CORPORATE AFFILIATE: U.S.Army-Res.Inst.Infec.Dis. Univ.North-Carolina
CORPORATE SOURCE: Virology Division, US Army Medical Research Institute of Infectious Diseases, Ft. Detrick, Frederick, MD 21702, USA.
JOURNAL: Am.J.Trop.Med.Hyg. (55, 2, Suppl., 216) 1996
ISSN: 0002-9637 CODEN: AJTHAB
CONFERENCE PROCEEDINGS: American Society of Tropical Medicine and Hygiene, 45th Annual Meeting, Baltimore, MD, 1-5 December, 1996.
LANGUAGE: English
ABSTRACT: An RNA replicon system for delivery and expression of genes in vivo, to induce protective immune responses, was developed from clones of attenuated Venezuelan-horse-encephalitis virus (VEE). Arena virus, bunya virus, filo virus, lenti virus and orthomyxo virus genes were introduced into VEE full-length RNA in place of VEE structural genes. Single or bipartite RNA helper encoding VEE capsid and glycoproteins was used to package replicons into replication-deficient virus-like particles (RepV). With bipartite RNA helper, no replication-competent VEEs were regenerated from replicon and helper RNAs. Safety was enhanced by short crossover regions between replicon and helper RNAs, mutagenesis of the VEE capsid autoprotease active center, a stop codon after the capsid gene, and attenuating mutations within E1 and E2 genes. The RepV delivered foreign genes in vivo, induced humoral responses to foreign proteins and conferred protection against parenteral or mucosal viral challenges. Immune responses and protection were not prevented by prior or subsequent inoculations of RepV with other genes. (0 ref)

48/3,AB/58 (Item 6 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs

0191256 DBA Accession No.: 96-02027 PATENT
Immune protection of subjects from disease- Venezuelan- equine-encephalitis virus vector-**mediated immunogen e.g. influenza virus hemagglutinin surface protein expression for use in recombinant** vaccine
AUTHOR: **Johnston R E** ; Davis N L; Smith J F; Grieder F B
CORPORATE SOURCE: Chapel Hill, NC, USA.
PATENT ASSIGNEE: Univ.North-Carolina 1995
PATENT NUMBER: WO 9532733 PATENT DATE: 951207 WPI ACCESSION NO.: 96-030338 (9603)
PRIORITY APPLIC. NO.: US 250445 APPLIC. DATE: 940527
NATIONAL APPLIC. NO.: WO 95US6739 APPLIC. DATE: 950526
LANGUAGE: English
ABSTRACT: A method of protecting a subject against disease is claimed, which involves administering a recombinant Venezuelan-equine-encephalit is (VEE) virus to the subject in an effective **immunogenic** amount, where the virus contains at least one attenuating mutation and a heterologous DNA segment (preferably at least 1 kb in length) containing a promoter operable in the subject operatively associated with DNA encoding an immunogen effective for protecting the subject from the disease. Also claimed are: (a) the DNA; (b) an infectious VEE virus RNA transcript encoded by the DNA; and (c) infectious VEE virus particles containing the RNA transcript. Preferred immunogens are those from the lenti virus, corona virus, flavi virus and influenza virus, especially the influenza virus hemagglutinin surface protein. The preferred promoter is the VEE virus 26S subgenomic promoter. Novel attenuating mutations are also disclosed. Advantageously, the heterologous insert can be relatively large (at least 1 kb in length). (32pp)

48/3,AB/60 (Item 1 from file: 342)
DIALOG(R)File 342:Derwent Patents Citation Indx

03703428 WPI Acc No: 00-013031/01
A composition for modifying mammalian cells, useful for stimulating immune response in cancer patients -
Patent Assignee: (UYNC-) UNIV NORTH CAROLINA
Author (Inventor): **MACDONALD G H ; MARTIN B K ; JOHNSTON R E** ; TING J P
Patent (basic)

Patent No	Kind	Date	Examiner Field of Search
WO 9951263	A2	991014 (BASIC)	

Derwent Week (Basic): 0001
Priority Data: US 81092 (980408)
Applications: AU 9937440 (990408); WO 99US7704 (990408)
Designated States
(National): AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG ; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US ; UZ; VN; YU; ZW
(Regional): AT; BE; CH; CY; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SL; SZ; UG; ZW
Derwent Class: B04; D16
Int Pat Class: A61K-039/00; C12N-005/10; C12N-007/01
Number of Patents: 002
Number of Countries: 083

Number of Cited Patents: 004
Number of Cited Literature References: 001
Number of Citing Patents: 000
?